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SOME RECENT ADVANCES IN NUTRITION

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A large part of human disease is chemical rather than bacterial in origin, and in diseases of chemical origin the trouble may be either excess or deficiency. Twelve case histories are here given to illustrate the fact that deficiency states resulting from poor diets are still important and sometimes puzzling. Mental symptoms disappeared when a man was finally treated with nicotinic acid for a long-standing dermatitis which was pellagra. A man of excessively frugal habits suffered from spells of increasing weakness; he was able to return to work after a series of hemorrhages led to the diagnosis of scurvy, which was remedied promptly by the oral administration of ascorbic acid. In many cases, however, the deficiency is more complex; the effect on the patient is a general biological blight, and a spectacular response follows the administration of complex foodstuffs such as nonfat dry milk solids. In some deficiencies anorexia and glossitis are prominent symptoms; breaking this vicious circle with folic acid in one case led to the appearance of a voracious appetite and the complete restoration of a patient who had been near death from severe macrocytic anemia. The body cells can recover to an amazing degree from these chemical upsets. The deficiency diseases bring crushing burdens and stark tragedies; their prevention is a significant part of actual medical practice.

TODAY GERMS ARE not our principal enemy. Our chief medical adversary is what I consider a disturbance of the inner balance of the constituents of our tissues, which are built from and maintained by necessary chemicals in the air we breathe, the water we drink, and the food we eat. Persons who are afflicted with "rheumatism" or "cancer," for example, are not the victims of germs but of altered chemistry. For a generation we have worked on the concept that our cells are never static and that in time they must be replaced in varying degrees by the nutrients obtained from food. More specifically, our working hypothesis has been that all disease is chemical and, when we know enough, chemically correctable.

Malnutrition or undernutrition may be either the cause or the result of ignorance and poverty. (More than half the population of the world is on the verge of starvation from lack of food.) Coexisting nutritional disorders complicate all the problems of the sick, and there seems little likelihood of a final solution of the great problems of medicine until we can obtain optimum nutrition. Great progress has been made in recent years, and it is gratifying to us to see that our recommended methods of coping with nutritional problems are being used so widely. If our efforts in years to come are to bring equally important information, we must think in broader terms and we must do so promptly. I can hear many saying, "Today Americans live better than ever before." It is gratifying to have had a part in creating this exciting era. Certainly the science of human nutrition is now on an immeasurably higher plane than we found it a

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Read in part before the General Scientific Meeting at the 106th Annual Meeting of the American Medical Association, New York, June 3, 1957.

himself. He drank some whiskey and rarely ate citrus fruit, vegetables, or lean meat. In fact, he did not remember the last time he had eaten any of these foods. For years he had what he called "ups and downs," periods of extreme weakness, and generally felt "no good." Prior to the appearance of the hemorrhagic areas shown in figure 3 he had had minor hemorrhages into his tissues from time to time. He responded promptly to 200 mg. of ascorbic acid administered orally three times a day. The hemorrhagic areas disappeared, his strength and feeling of well-being increased, and within three weeks he was able to return to work. We advised him as to what foods he should eat; he followed instructions and has not had a relapse since.

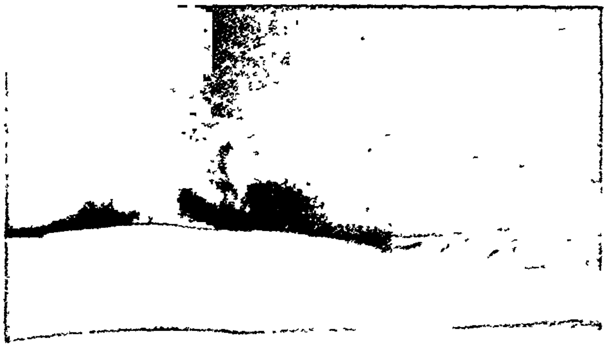


Fig. 3 (case 3).—Hemorrhage into tissues of man with scurvy.

The prompt disappearance of the vague symptoms of ill health in this patient after ascorbic acid therapy suggests the necessity of early treatment and of prompt and adequate treatment.

Case 4.—Figures 4 and 5 show the nails and face of a woman who for many years had had excess menstrual bleeding and had eaten a poor diet. Her general pallor and the appearance of her fingernails suggested an underlying iron deficiency. After eight months of treatment with ferrous sulfate, her nails were almost normal and she was strong enough to work again. An interesting feature of this case is that she had had a poor diet and periods of menstrual hemorrhage for years. Because some of the previous observers noticed the severe anemia, weakness, but lack of low color index, they gave her intensive therapy with folic acid and vitamin B_{12}. Needless to say, a disturbance due to a lack of iron did not respond.

A deficiency of iron, of course, frequently is the cause of anemia in women and in children. It is important to maintain proper hemoglobin values throughout the latter part of infancy; however, many times iron is not taken in adequate amounts or frequently enough because it is not readily acceptable to the young. Also, the physician often fails to think about it.

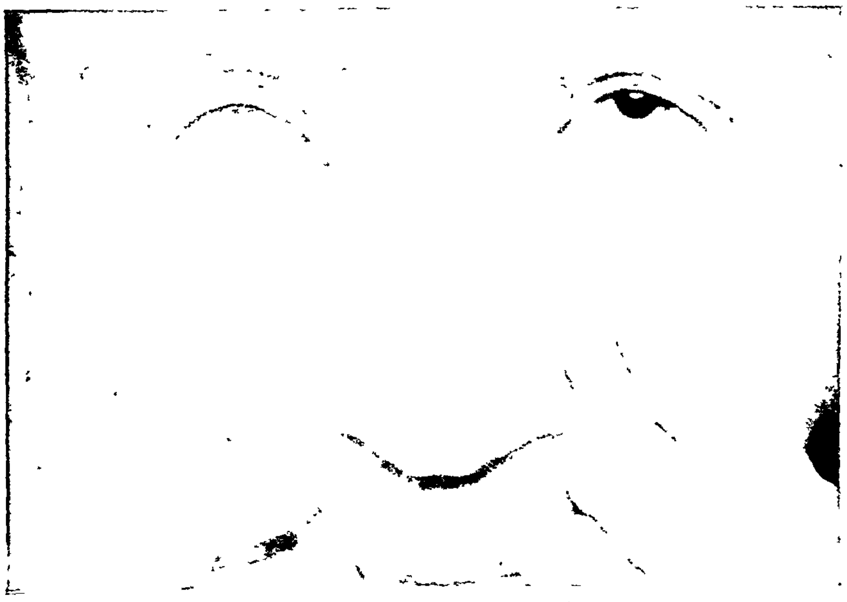


Fig. 4 (case 4).—Face and nails of woman with iron deficiency.

Diagnostic Significance of Lesions Affecting Oral Tissues

The response of the alimentary tract to inadequate diets never has been studied as much as it deserves. The tissues lining the cavity of the mouth are easily examined and the examination causes no discomfort to the patient. In our 30 years of studying deficiency diseases, my associates and I have been impressed by the frequent appearance of lesions in the mucous membranes of the oral cavity, tongue, and gingivae. In a series of 914 consecutive patients admitted to the Nutrition Clinic of the Hillman Hospital, Birmingham, Ala., the presenting symptom in 329 of these patients was soreness of the mouth and tongue.[1] From the point of view of their specific chemical etiology, the lesions affecting the oral tissues frequently are mixed and in many instances a number of therapeutic agents are required for complete treatment. Because of the similarity of some of the lesions due to a deficiency of nicotinic acid, vitamin B_{12}, or folic acid, specific diagnosis is difficult.

Case 5.—Figures 6 and 7 show the tongue of a patient with vitamin B_{12} deficiency before and after treatment with vitamin B_{12}. Figure 6, taken before treatment, shows the redness and swelling of his tongue and cheilosis. The area of low-grade infection at the side of his tongue was caused by trauma which resulted from his biting his swollen tongue. On this occasion he was treated with vitamin B_{12} and intrinsic factor orally. As shown in figure 7, taken three weeks later, his tongue was no longer thick and red, the papillae had regenerated, the area of low-grade infection had disappeared, and the cheilosis had almost healed. On a previous occasion we had treated him with liver extract intramuscularly and on another occasion with vitamin B_{12} administered intramuscularly. The response of the tissues was the same in each instance.

Just as figures 6 and 7 show the typical response of glossitis caused by a deficiency of vitamin B_{12}, figures 8 and 9 show the typical response of glossitis due to folic acid deficiency. The appearance of the tongue, the inflamed oral mucous membranes, and the redness at the angles of the mouth were similar to the previous case.

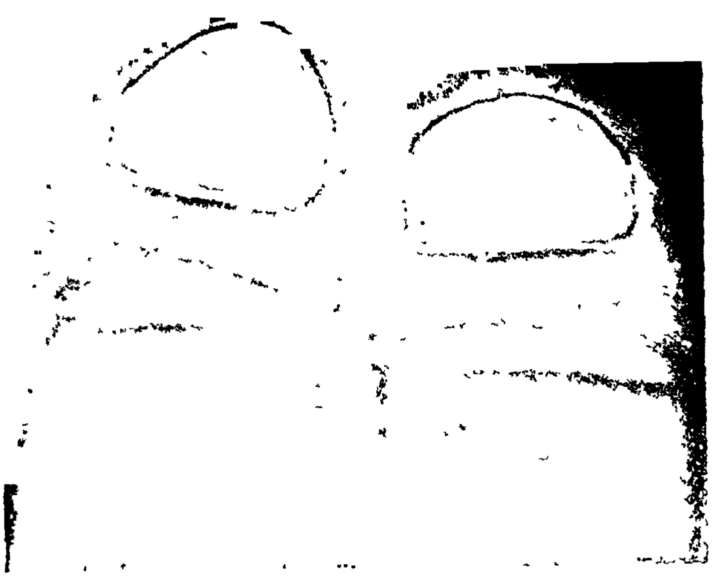


Fig. 5 (case 4).—Nails of woman with iron deficiency.

Case 6.—This patient with a typical case of severe macrocytic anemia of "pernicious anemia" type (tropical sprue) in relapse was treated with folic acid by my Latin American associates and me. He was too weak to walk and had to be carried into the hospital, and he was so near death that he could be aroused only with some difficulty. He was mumbling incoherently and refused all food. This particular illness was of several months' duration, although the exact duration was indefinite. Previous attacks of diarrhea had persisted for several weeks, during which time he had had to be cared for by others, and he had been unable to work regularly for several years. Figure 8 illustrates the pallor and slickness of his tongue. At the time this picture was taken his hemoglobin level was only 19%, his red blood cell count was 1,520,000 per cubic millimeter, and the reticulocytes 0.2%. His stools were large, liquid, whitish yellow in color, and foul-smelling. He had megaloblastic arrest of the bone marrow. We gave him 10 mg. of folic acid orally daily. Within 48 hours he began to feel much better. He was mentally alert and sat up in bed and asked for food. Within 96 hours his appetite was voracious and he sat in a chair beside his bed most of the day. On the seventh day of therapy the reticulocytes peaked at 28% and a rapid increase in red blood cells and hemoglobin followed. After six days on therapy his tongue was covered with normal papillae (fig. 9). The frequency and volume of his stools decreased on the third day of therapy. The diarrhea continued to subside, and by the 12th day his stools were normal. After 21 days on therapy his hemoglobin level had increased to 52% and his red blood cell count to 2,790,000. By this time he had gained 12 lb. (5.4 kg.) in body weight. At the time he was discharged he was given instructions in regard to a proper diet, and in the following six months he gained 50 lb. (22.7 kg.) in body weight. He has remained well and has worked steadily.

It is important to realize that this patient would have responded in an identical manner had he been given injections of vitamin B_{12}.

Case 7.—Figure 10 is shown because this woman with typical pellagrous glossitis never developed pellagrous skin lesions. In addition to the glossitis, she also developed a psychosis. Some physicians do not understand pellagra *sine* pellagra, and, having in mind the criteria that pellagra should be associated with dermatitis, the physicians previously concerned with this case did not make the diagnosis of pellagra when no dermatitis was present or did not appear, with the result that she became steadily weaker. The severity of the psychosis increased to the point that her family was considering having her committed to an institution. After treatment with 50 mg. of nicotinic acid orally 10 times daily, the glossitis was relieved and her mental disturbances disappeared. She was given advice in regard to a proper diet, and soon she was able to do her housework and take care of her family.

Many of our talented teachers in the field of nutrition who have had relatively little experience in combating widespread endemic dietary deficiency disorders believe and teach that these deficiency syndromes are due to the lack of a specific nutrient and can be quickly overcome by the administration of that specific nutrient. Working many years in direct daily contact with the problem has taught us that dietary deficiency disorders arising from a lack of the vitamin B complex do not occur singly but as mixed deficiency diseases.[2] The pattern of these disorders is different from person to person and even among individual members of the same family who may eat at the same table. There

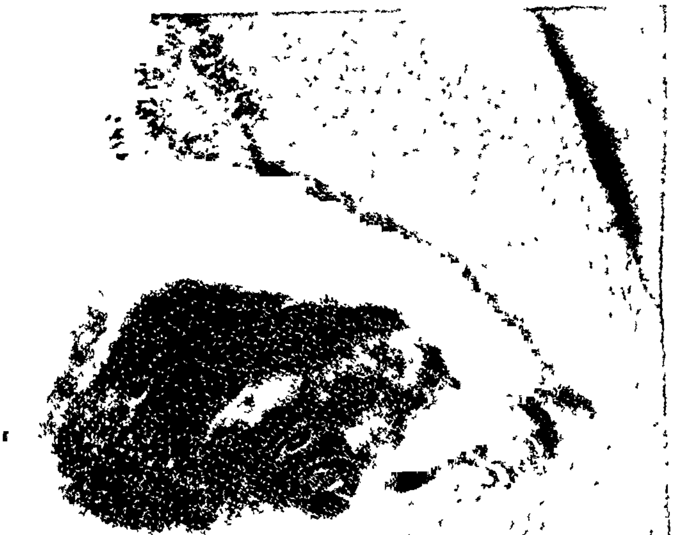


Fig. 6 (case 5).—Tongue of patient with vitamin B_{12} deficiency before treatment with vitamin B_{12}.

is such extreme variability in the presenting symptoms and in the secondary and even tertiary lesions which arise that many years ago we advocated mixed vitamin therapy for treatment and for prevention. This has been extremely effective, except in areas where the teaching is so strongly in favor of giving a single nutrient. In such instances rather atypical lesions, such as shown here, frequently are not recognized for what they really are and often the nutrient needed to correct the deficiency is not given and the results for the patient and for the physician are most unsatisfactory.

The purpose in showing these lesions which tend to be more easily diagnosed than the average and less complicated in their clinical manifestations is to stress the point that one's working hypothesis, however scientific, is not successful in bringing about gratifying results unless the damaged tissues of the sick person receive the essential nutrients needed to restore them. At the present time in the practice of medicine in the United States, vitamins are much more appreciated and accepted than they were some years ago. Patients receive them in large amounts, with the result that the physician seldom sees lesions such as these we described. This has been one of the great advances in vitamin therapy. It has been gratifying to see that a vast group of practitioners who a few years ago were using these essential nutrients for the treatment of specific disease states are now using them to maintain health, strength, and vigor.

Adequate Nutrition During Growth Period

For 30 years I have been interested in the importance of nutrition in the health of the individual, beginning with conception and ending with death. For nearly 20 years we have been studying intensively the insidious effects of sustained substandard nutrition, the so-called hidden hunger, on the growth of infants and children.[3] Our working hypothesis has been that the events of the growth period may determine to a considerable extent a person's subsequent health. (In our experience gross changes certainly affect the health for a long period of time.) The so-called subclinical changes are subtle and their detection requires unusually sensitive methods.

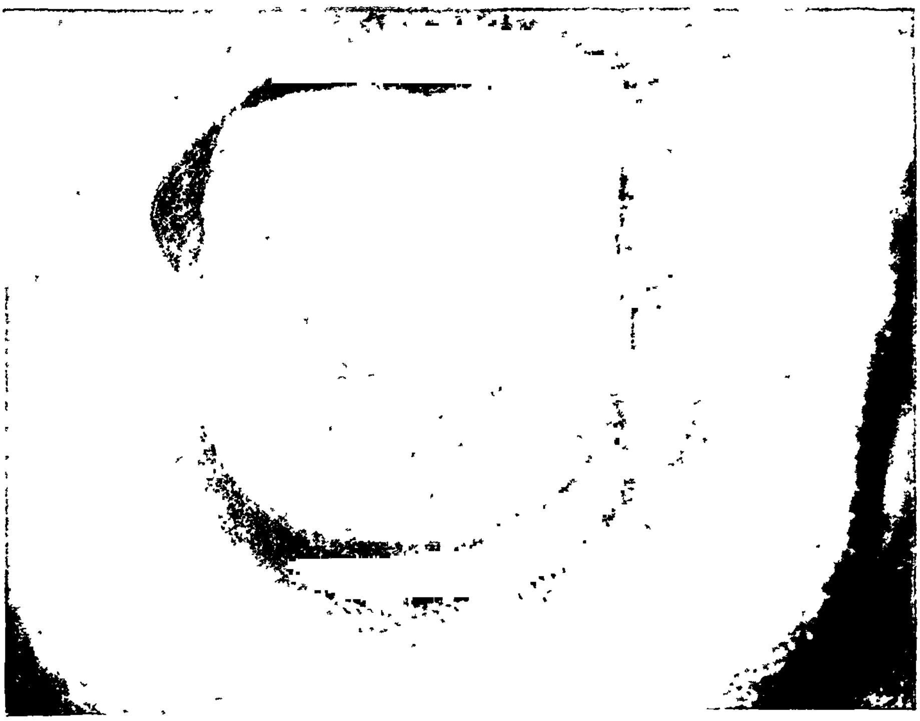


Fig. 7 (case 5).—Tongue of patient with vitamin B_{12} deficiency after treatment with vitamin B_{12}.

One of our studies of approximately 1,000 undernourished children indicates that the following stigmas are interrelated with the process of human nutritive and growth failure: (1) tortuous, erratic growth curves which lead to a failure to attain expected weight and height, (2) repeated episodes of retarded growth which follow a seasonal pattern recurring every spring and summer; (3) early onset of measurable growth failure such that a significant lag is present by 3 years of age; (4) slow rate of skeletal maturation; (5) high degree of asymmetry in the development of component parts of the skeleton; (6) high frequency and variety of anomalous bone centers; (7) persistence of radiopaque transverse lines in the shafts of the long bones indicative of disturbed bone metabolism; and (8) delayed appearance of postnatal ossification centers and fusion of epiphyses with shafts.

Our goal then is to determine the optimal conditions of the growth of a child so that he attains his maximum physical and mental development. Of all the factors which influence growth, none is more restrictive than time. As physicians know, time sets the limit within which physical growth must be completed. The time allotted for growth, though, may vary from child to child, but any growth debt which may have accumulated prior to the fusion of the epiphyses and diaphyses of the major long bones must be removed if maximum physical development dictated by his inherent growth pattern is to be achieved.

Maximum physical development reflects maximum performance at the cellular, tissue, and organ level. The body processes are so integrated and so dependent upon an adequate supply of essential chemical substances contained in foods that an absence or deficiency of any one important factor may impair the efficiency of a whole chain of reactions, each of which affects the health of the child. For example, in our studies dealing with the growth-promoting properties of various supplements in children with nutritive failure, we noted that growth of these children was, in general, accelerated by a proper supplement. Let us see how this works by presenting a brief summary of a representative case of nutritive failure in a child.

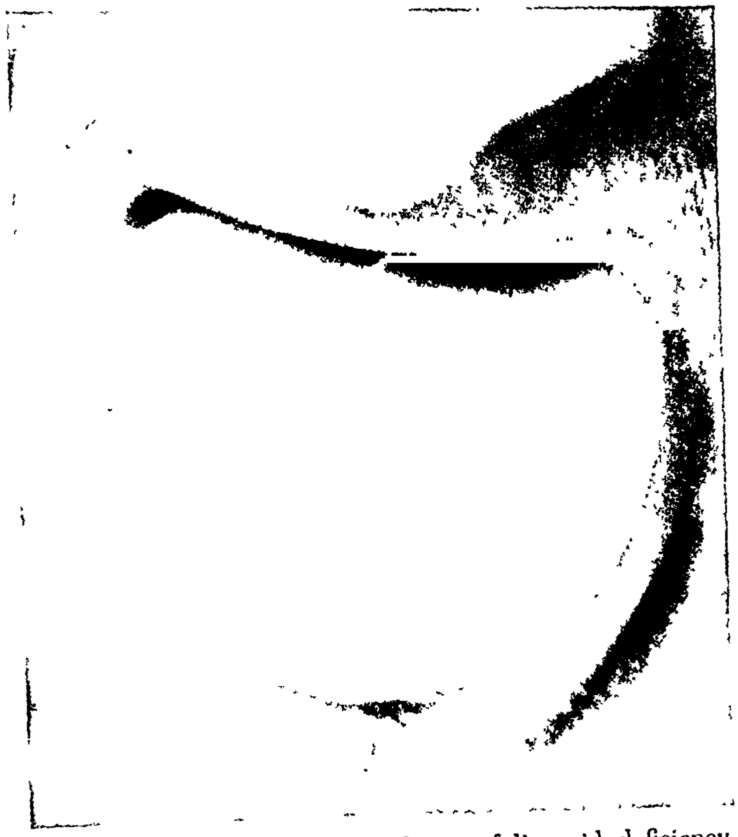


Fig. 8 (case 6).—Glossitis due to folic acid deficiency, before folic acid therapy.

CASE 8.—A 7-year-old boy was brought to the Nutrition Clinic of the Hillman Hospital by his mother in October, 1953, because "he isn't growing properly." The family history brought out that the father was the only wage earner and worked irregularly making and sacking charcoal, a trade he learned from his father and which he, in turn, was teaching his sons. The mother was industrious as far as her health allowed and she had a clean home and a small garden. There was no evidence of familial disease.

He was the second of four children in a family of three boys and one girl. He was delivered at term and weighed 9 lb. 11 oz. (4,394 Gm.) at birth. He was breast-fed for one month and then given a formula. Solid foods were started at 15 months of age. Orange juice was given frequently beginning at one month of age; cod liver oil was not offered. He sat alone at 4 months of age; he cut his first tooth, walked, and talked at one year of age. He had the usual childhood illnesses and, in addition, from time to time had "trouble with his skin."

The physical examination made just prior to supplementation showed a fairly well-developed, somewhat undernourished boy with a protuberant abdomen. Except for slight scarring at the angles of the mouth and enlargement of the tonsils, no abnormal physical findings were demonstrated. The regular laboratory determinations were negative. Roentgenograms of the left hand and wrist taken every six months showed an increasing retardation in skeletal maturation. His diet, which was studied frequently, showed that his food intake was relatively high in carbohydrates and refined fats and low in protein, calcium, thiamine, nicotinic acid, and calories.

After three years of intensive study, we selected him to receive a dietary supplement of reconstituted nonfat dry milk six days a week for six months, since we had adequately determined that he had chronic nutritional deprivation and increased lag in developmental and skeletal age. At the time of his selection he had a lag of 4 months in developmental age (Wetzel) and of 22 months in skeletal age (Todd).[4]

In addition to his regular diet during the six-month period of supplementation, he was given 6 oz. of Carnation Instant Nonfat Dry Milk Solids daily. This amount was arbitrarily chosen because its nutritional value equals approximately two quarts of skim milk (we mixed it with only 10 oz. of water because we knew his stomach was not large). It was prepared daily in our laboratory and given by one of our workers who recorded his intake. He could and did take each feeding well. In fact, his mother volunteered "he likes it so much he always drinks all of it." This boy is one of a series of children to whom we have given the Carnation Instant milk product. We were interested in testing this new product when we learned that it had been altered to make it instantly soluble in cold water, and that its acceptability over other products available at the time was increased. Naturally, as investigators, we wished to learn if the changes which increased the solubility and palatability had so altered the milk that it would not relieve the underlying general nutritive failure. We wished to know how this milk would affect the children when given as a supplement to their basic diets. Since we did not wish to depend on published reports, we chose to make complete chemical and biological assays. Our results are very similar to those published.

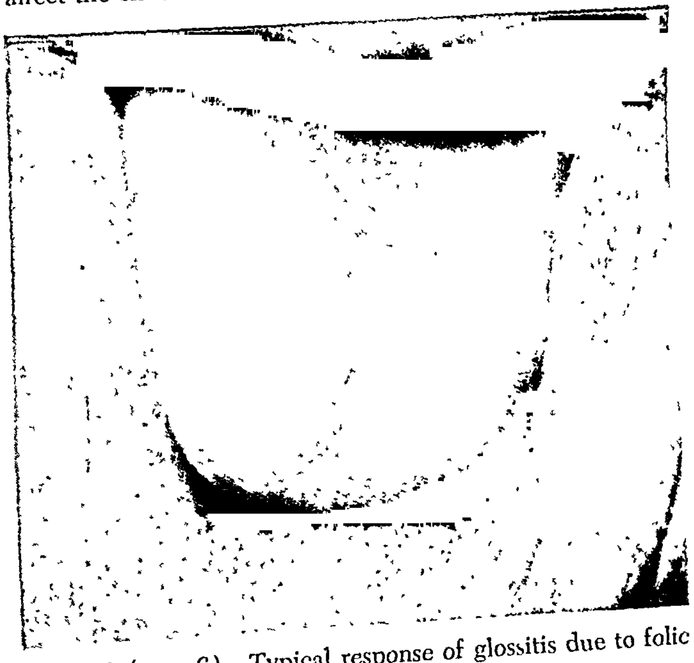


Fig. 9 (case 6).—Typical response of glossitis due to folic acid deficiency, after folic acid therapy.

This boy's response, like that of the others in the series, has been spectacular. Six months after supplementation was initiated, his lag in developmental age had been reduced

50% and his lag in skeletal age had been reduced over 60%. As can be seen in figure 11, he had been growing rather slowly but with the supplement his growth rate was tremendously accelerated, which, of course, accounts for his paying so much of his "debt" in the short period of six months. If you think this is remarkable, you should see how his general physical status and performance improved. Instead of being "fractious" and unwilling to play with other children, he became very much one of the group. His teacher stated "he changed from a surly, backward pupil to one who is responsive and interested in his schoolwork."

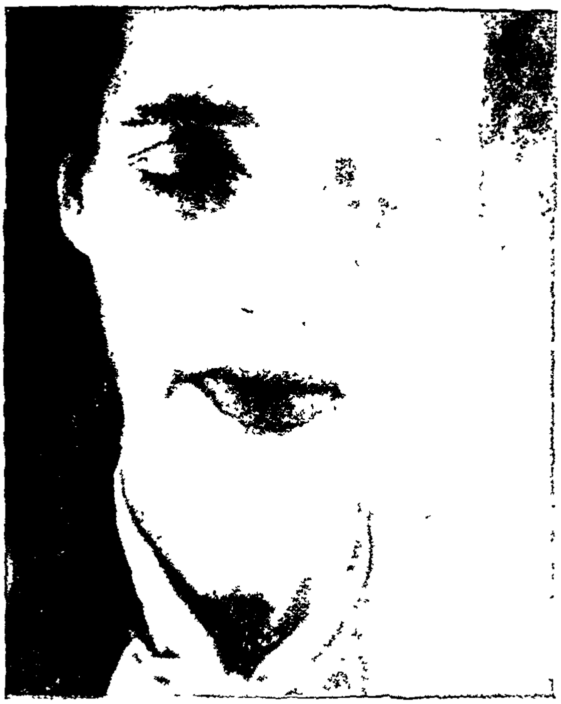


Fig. 10 (case 7).—Woman with typical pellagrous glossitis, without pellagrous skin lesions.

For almost a generation now we have recognized that, when diets of an area are deficient in the nutrients essential for life, the response is a general biological blight affecting people and animals. Accordingly, it was decided to test further the biological response to this particular milk preparation by feeding the nutritional equivalent of the diet consumed by the patient in case 8 to each of 30 male, albino, Sprague-Dawley rats. The test diet was based on the results of analysis of repeated diet histories obtained over a three-year period which immediately preceded the selection of this patient for supplementation. The diet contained 18% lard, 19% granulated white sugar, 35% enriched, degerminated white corn meal, and 28% enriched white wheat flour. Each rat was given this diet ad libitum for a period of 20 weeks beginning at 6 weeks of age. Each was killed, autopsy was performed, and histological studies were done. Each rat was compared with its counterpart from a group of the same age, sex, and strain maintained on the test diet supplemented with Carnation Instant Nonfat Dry Milk Solids.

The test diet without the supplement exerted a striking retarding influence on the somatic, sexual, and skeletal growth of the young white rats. The effect on somatic growth is shown in figure 12. Although both rats were the same age, the larger rat, representative of the group on the test diet plus supplement, weighed 419 Gm., whereas the smaller rat, representative of the group on the test diet alone, weighed only 125 Gm. The gross and microscopic manifestations of retarded sexual growth of those receiving only the test diet are illustrated in figures 13 and 14. Each of the rats given only the test diet had testicular atrophy, arrested spermatogenesis, and priapism, whereas none of the group receiving the supplement showed these changes. The inability of the test diet to support proper bone growth is seen in figure 15. In the rat given the supplemented diet the distal metaphysis of the radius is undergoing the sequential conversion of growth cartilage into bone, whereas the rat on just the test diet shows the typical cessation of chondrogenesis and osteogenesis noted in this group. The nutritionally deficient character of the test diet was demonstrated not only by its failure to support growth in the young rats but by the great prevalence of deficiency lesions of varying degrees of severity which were encountered in these

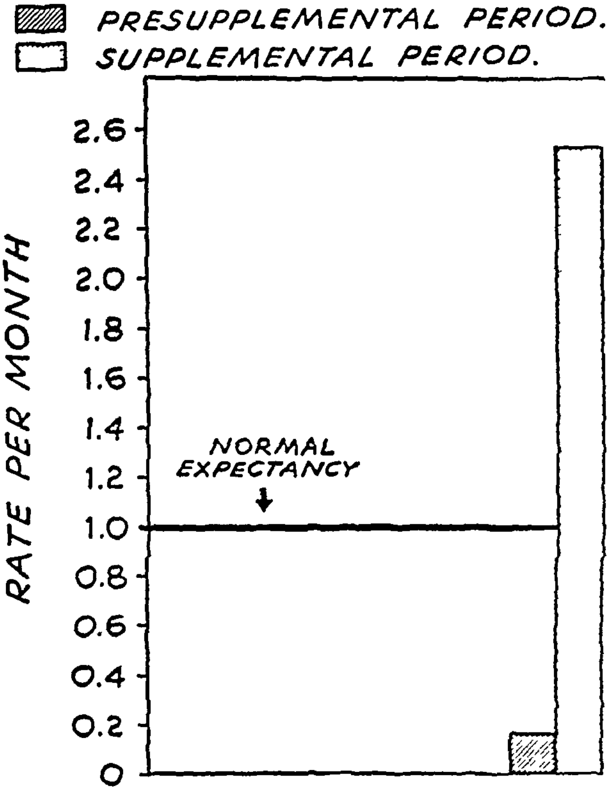


Fig. 11 (case 8).—Contrast between growth rates (Todd) during presupplemental period and supplemental period.

Specifically these included fatty liver (fig. 16), dacryohemorrhea (bloody tears) (fig. 17), dry, coarse hair, alopecia, and dermatitis.

For many years we have been relating nutrition directly or indirectly to nearly all the diseases and ills of man. We hope that certain observations which we have made on children will serve as the groundwork for a complete chemical evaluation of the human growth process. At present we have only a thread of the information necessary for an understanding of the complex process of the growth and development of children.

Fig. 12.—Small rat, restricted to deficient diet eaten by child in case 8, contrasted to larger rat, a litter mate which was given test diet plus milk supplement.

Claude Bernard emphasized that the living person must be treated as a harmonious whole. It is interesting that the growth of many of our organ systems can proceed at different rates and yet be normal. Nevertheless, there is an underlying orderliness of these processes, and it is with the measurement of some of these processes that we are directly or indirectly concerned. Let us give an example of an entirely different medical problem and its effect on the health of the child.

CASE 9.—A 22-year-old white female was brought by her mother to the Nutrition Clinic of the Hillman Hospital when she was 7 years of age. The mother, who had been treated in the Nutrition Clinic for pellagra and other deficiency diseases, was concerned about her daughter's health. She said that the child was "well nourished but she doesn't eat well and is nervous and doesn't feel like playing with the other children." She appeared to be extremely anxious and hypersensitive. There was typical pellagrous dermatitis around both ankles. The child was treated properly and responded well. We decided to study her growth progress, and thereafter measurements, radiographs, and dietary assessments were made at regular intervals. In June, 1943, when she was 8 years 2 months of age, she contracted typhoid. She was confined to bed for four weeks during which time she lost weight. We made certain, however, that she continued to eat properly and that she received ample vitamin supplements during this period of time.

People observing her were impressed with the fact that she recovered without serious complications; however, we had long been studying the effects of infectious processes, such as tonsillitis, appendicitis, and childhood diseases, on the metabolic processes of the body and knew that the prognosis was good. In our lectures we have always stressed that the metabolism of the body is never static, that the nutrients tend to ebb and flow, so to us the effect on her bone and over-all body growth, as indicated by general measurements and plotting on the Wetzel grid (fig. 18), was not surprising. As can be seen in figure 19, the effect on the bone was reflected by the deposition of a heavy transverse radiopaque line in the distal end of the shaft of the radius which required more than three years to disappear completely. The channel and auxodrome curves on the Wetzel grid were characterized by abrupt declines coincident with the period of illness. The preinfection points were reattained nine months after the onset of the disease.

This case demonstrates the sensitivity of a child's growth to an acute infectious process. We know from the study of literally thousands of cases that unless the food intake is quantitatively and qualitatively sufficient to remove the growth debt incurred by the disturbed nutrition and metabolism accompanying an illness, as well as to provide the wherewithal for normal body increment, the child will never achieve his maximum growth potential.

Nutrition in Adult with Acute or Chronic Disease

So much for a glimpse of the effect of disease on the nutritional status of the young and growing person. Now let us turn for a moment to a brief discussion of the relation of proper nutrition to the mature person who develops acute or chronic disease. In my opinion, all severe disease processes affect the metabolism of the tissues and, therefore, the nutrition of the tissues, but arbitrarily I shall select rheumatoid arthritis to discuss with you in order to present a way of thought. As physicians,

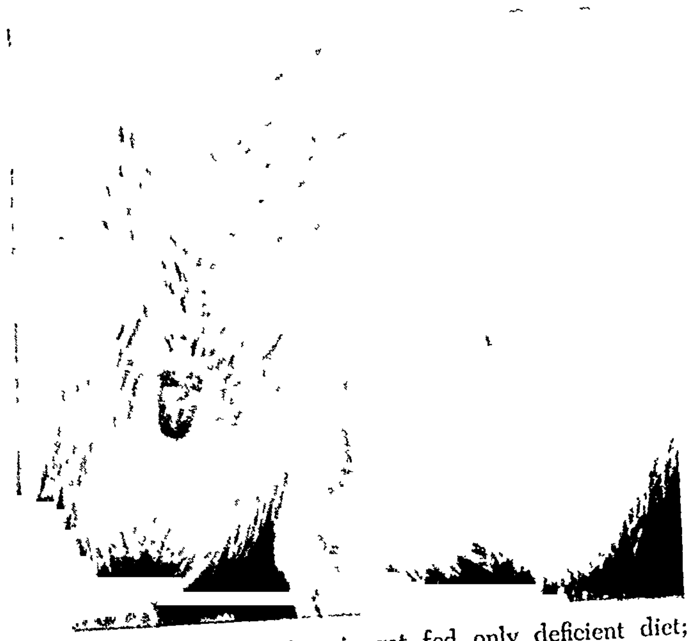


Fig. 13.—*Left*, priapism in rat fed only deficient diet; *right*, rat fed same diet plus milk supplement.

you know that "rheumatism" is the great crippler, yet it kills relatively few. In the United States the number of persons afflicted with "rheumatism" is greater than the total number of persons with heart disease, cancer, poliomyelitis, diabetes mellitus, and tuberculosis. One of the projects on which we have worked is how to devise methods of keeping people with rheumatic disorders on the job.

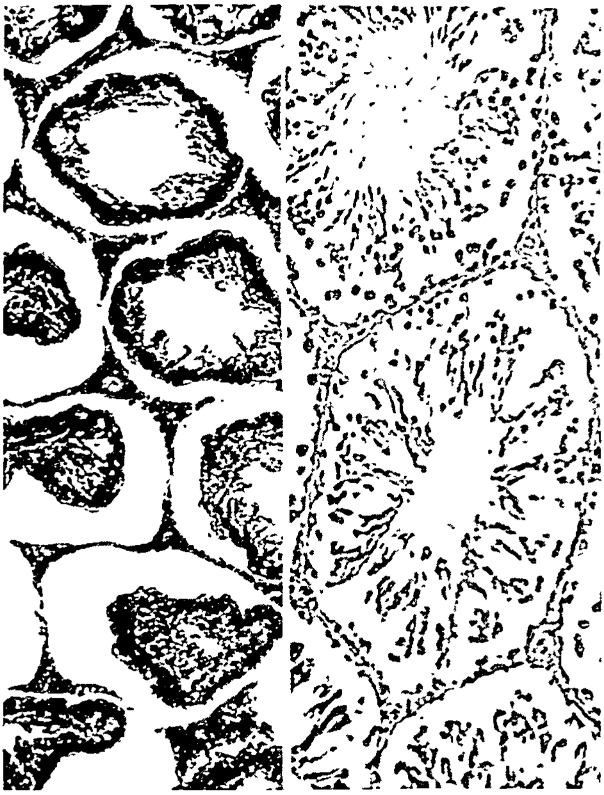


Fig. 14.—Photomicrographs (same magnification in each) of sections of rat testes. *Left,* from rat fed test diet; *right,* from rat given test diet plus milk supplement. Note spermatogenesis in rat given supplement and its absence in rat fed only test diet.

In the course of investigating new therapeutic agents or devising new methods to use old therapeutic agents, we carefully study their effects on the nutritional status of the patient. The proper use of these therapeutic agents and foods may mean the difference between a useful life and a useless life, between a long life and an early death. Accordingly, the responsibility of the physician is overwhelming. A number of times we have published our observations on the striking decrease in toxicity from disease and increase in food intake after the administration of pituitary ACTH, cortisone, or one of the related steroids to persons with rheumatic disorders.[5] Since the salicylates also are very effective therapeutic agents in many persons with such disorders, from a nutritional point of view it seemed important to check their effect singly and in combination with antiarthritic steroids (cortisone, hydrocortisone, methylprednisolone [Medrol], prednisolone, prednisone, and triamcinolone [Aristocort]). In properly selected patients the salicylates or the salicylates and the antiarthritic steroids have had a profound beneficial effect characterized by the prompt amelioration of the pain, stiffness, and swelling. None of these agents are specific in their therapeutic effect, and at termination of treatment there frequently is recurrence of pain, tenderness, and stiffness. For the moment let us not consider the usual symptoms associated with rheumatic disorders but let us think of the nutritive status of people who have these conditions. We find that they may be obese and actually need a calorie reduction, though many of those who are obese may be deficient in proteins and vitamins. Many are generally undernourished and, of course, need the best possible diet. Some have typical deficiency disorders and, in order to rehabilitate them, these deficiency states have to be treated. There are many more who have a mild degree of nutritive failure.

Many rheumatologists now look for nutritive failure among the patients who have arthritis and other debilitating diseases. Aspirin alone or aspirin with a small amount of one of the steroids, as we have shown, plays an important role in the nutrition of patients (fig. 20). Many of these patients are

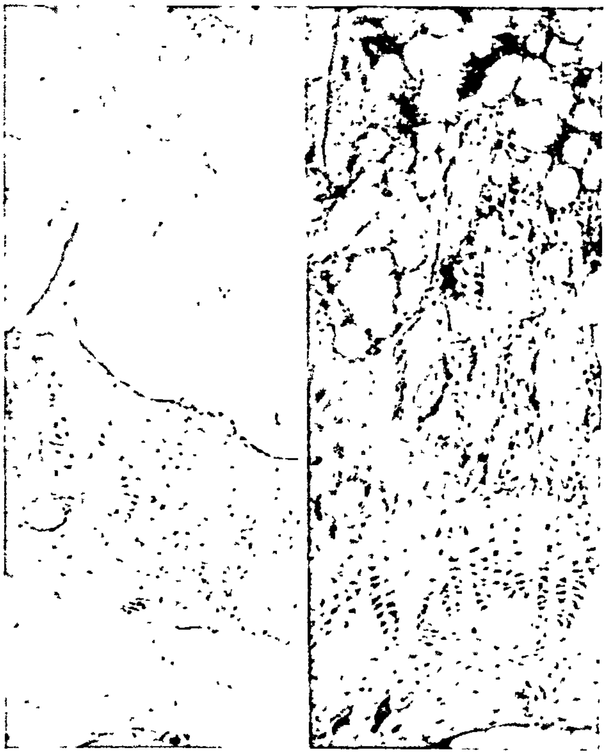


Fig. 15.—Bone sections from rats from same litter. *Left,* poor bone development in rat fed only test diet; *right,* normal bone development in rat fed this diet plus milk supplement.

so depressed that their morale is low and they lose their desire to eat. Some of them are actually so incapacitated that they cannot earn money to purchase food. Many who have food will not eat, and some cannot eat because the arthritis affects the joints of the jaws so they cannot even open their mouths. Others have nausea and vomiting, with the result that absorption is decreased. An example of one facet of the relation between disease and inadequate nutrition is demonstrated by the following brief case history.

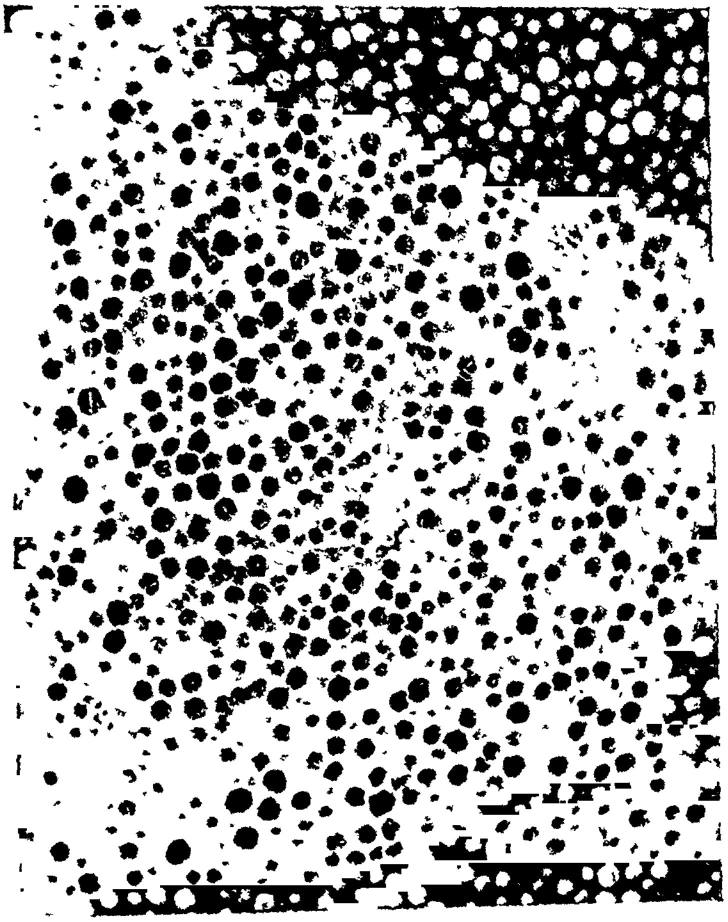


Fig. 16.—Section of fatty liver from rat on test diet.

Case 10.—A 60-year-old white worker was sent to the Nutrition Clinic of the Hillman Hospital in an ambulance in 1950. We found his joints swollen and the muscles and joints excruciatingly painful. He was unable to walk or even stand alone, and it was obvious that he was severely ill. His temperature ranged from 101 to 105 F (38.3 to 40.5 C).

Later we learned that when he was a small boy his legs ached a great deal, and during the winter months they ached until he "felt they would bust." His mother gave him relief by warming a flannel blanket and wrapping his legs in it. Fifteen or 20 years prior to 1950 he had some pain and swelling of the ankles on a few occasions. This was not very severe and disappeared when a "pharmacist" gave him a liniment which he rubbed on them. When questioned about aspirin or any medication by mouth, he said he had not taken aspirin because he thought that it was only for headaches and that "it might be dangerous."

Three weeks prior to the time we first saw him, he suddenly developed acute pain in his left foot and ankle which soon spread to all his joints. He stated that each day the joints became "hotter," more swollen, and more tender. The pain could not be controlled by codeine or morphine so that any movement caused him unbearable pain and he could not refrain from crying out. He lost his desire for all foods and "just lived on coffee." He knew that he had lost several pounds in body weight, although he did not know exactly what his weight loss was. He was admitted to a hospital and given injections of penicillin and morphine. He did not improve and was referred to our clinic by his physician.

When we first saw him, his temperature was 101 F. The physical findings were negative except for general weakness, great swelling of his ankles, and tenderness all over his body. His erythrocyte sedimentation rate was 59 mm. per hour (corrected). A diagnosis of acute "rheumatism" was made, and he was given large doses of cortisone and aspirin. We decided to allow him to go home. He was advised to move about as much as possible, and he and his wife were instructed in regard to his treatment, diet, and general care. Within 24 hours after therapy was started he volunteered that he had obtained great relief; four days later he got out of bed, made coffee for himself and his wife, and ate a big breakfast. This was the first time in many days that he had been able to get out of bed or to eat. On the fourth day of therapy his temperature was normal. After 22 days of treatment at home there was no limitation of movement of any of his joints, all the pain and swelling had disappeared, and he walked without difficulty. He said, "I feel so good I want to get back on the job. I'm eating so much I'll get fat if I don't work it off." He returned to work and has not missed a day since. At times he has had some aching in his ankles, hands, and shoulders and swelling of his ankles and hands. In every instance the recurrence of these symptoms was associated with a lack of desire for food. Prompt relief followed the administration of three to four 5-grain (0.3-Gm.) aspirin tablets every four to six hours, except on four occasions when this did not prove to be, in his own words, "strong enough." On three of these occasions we gave him the same amount of aspirin in the form of "Cordex," a preparation which also contains prednisolone. This material has been "strong enough" to give him prompt relief of pain which is associated with a return of his desire for food and a decrease in the swelling of his joints (fig. 21). On the occasion of the fourth relapse we gave him a mixture of aspirin (the same amount as mentioned above) and prednisone. The administration of this preparation called Co-Deltra was also followed by prompt relief of symptoms and an increase in desire to eat.

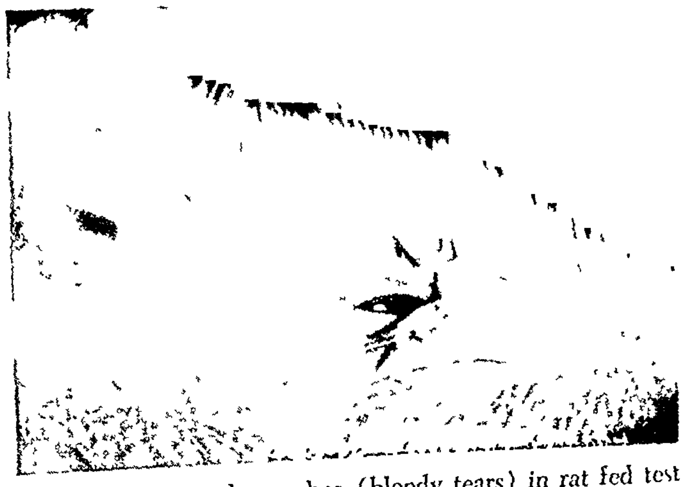
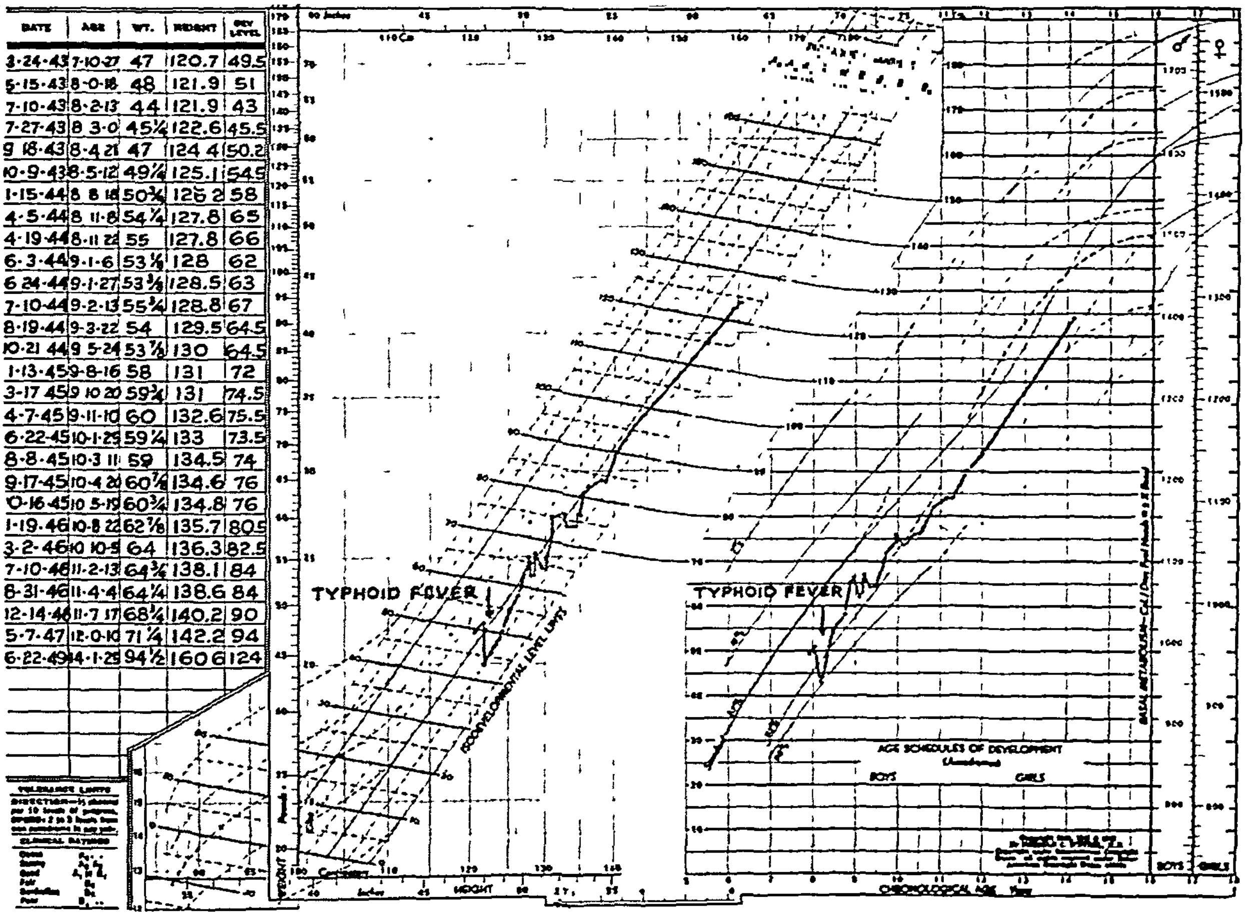


Fig. 17.—Dacryohemorrhea (bloody tears) in rat fed test diet.

This case is representative of patients with acute or chronic disease in which the disease and the pain are such that they do not eat properly. When the disease is brought under control, they do eat. We have shown how the intensity of the disease varies and also how this patient's job was saved for him by prompt therapy. In the past seven years he has maintained his nutritional status, strength, and vigor and has been able to work every day with a minimum of treatment.

The majority of persons with severe rheumatic disorders are more difficult to treat than this patient because their disease lingers on day after day and it is a problem to get them to eat properly. It can be done, however, by individual attention, by prescribing proper mixtures of vitamins when indicated, and by giving adequate amounts of salicylates alone or combined with steroids. The importance of eating a proper diet must constantly be pointed out to the patient. Over and over again we have seen persons with acute or chronic disease develop coexisting nutritional disorders.



DATE	AGE	WT.	HEIGHT	DEV LEVEL
3-24-43	7-10-27	47	120.7	49.5
5-15-43	8-0-18	48	121.9	51
7-10-43	8-2-13	44	121.9	43
7-27-43	8 3-0	45¼	122.6	45.5
9 18-43	8-4 21	47	124 4	50.2
10-9-43	8-5-12	49¼	125.1	54.5
1-15-44	8 8 16	50¾	126 2	58
4-5-44	8 11-8	54¼	127.8	65
4-19-44	8-11 22	55	127.8	66
6-3-44	9-1-6	53⅛	128	62
6 24-44	9-1-27	53⅜	128.5	63
7-10-44	9-2-13	55¾	128.8	67
8-19-44	9-3-22	54	129.5	64.5
10-21 44	9 5-24	53⅞	130	64.5
1-13-45	9-8-16	58	131	72
3-17 45	9 10 20	59¾	131	74.5
4-7-45	9-11-10	60	132.6	75.5
6-22-45	10-1-29	59¼	133	73.5
8-8-45	10-3 11	59	134.5	74
9-17-45	10-4 26	60⅞	134.6	76
10-16-45	10 5-19	60¾	134.8	76
1-19-46	10-8 22	62⅞	135.7	80.5
3-2-46	10 10-5	64	136.3	82.5
7-10-46	11-2-13	64¾	138.1	84
8-31-46	11-4-4	64¼	138.6	84
12-14-46	11-7 17	68¼	140.2	90
5-7-47	12-0-10	71¼	142.2	94
6-22-49	14-1-29	94½	160 6	124

Fig. 18.—Grid for evaluating physical fitness in terms of physique (body build), developmental level, and basal metabolism—a guide to individual progress from infancy to maturity.

The response of patients with megaloblastic anemia to cortisone, hydrocortisone, prednisolone, and prednisone has been described by our group from time to time.[6] The initial fall of the serum-iron level, which is always seen early in the successful treatment with vitamin B_{12} or folic acid, is not observed with these steroids. These patients have a satisfactory clinical and hemopoietic response and an increase in reticulocytes followed by an increase in red blood cells and hemoglobin. This response, if enough material is given, follows through until the bone marrow is restored to a normoblastic state. My associates and I have shown recently that triamcinolone and methylprednisolone produce similar results. All six of these steroids were given by mouth.

We do not recommend these materials for the treatment of any form of megaloblastic anemia that will respond to vitamin or nutritional therapy. The precise roles of folic acid and vitamin B_{12} in converting megaloblastic to normoblastic bone marrow is not understood, and the role of the steroids is still less understood. Some of the hematologists and rheumatologists, who certainly would wish to treat their "rheumatics" nutritionally when necessary, should have drawn to their attention the danger of suppressing unsuspected megaloblastic anemia in their patients. Is it not remarkable that these substances which relieve inflammatory reactions, allergic reactions, and so forth can stimulate hemopoiesis under certain circumstances? While they suppress arthritis or allergy, for example, they may also produce blood regeneration; yet there still would be a fundamental lack of essential nutrients in the tissues. There is no reason to think that the steroids relieve acute combined degeneration of the spinal cord. It behooves the physician treating chronic diseases to insure proper and complete nutrition for his patients. Millions of persons who have these disorders demand and deserve our help, as do the millions who have minor aches and pains.

The study of minor aches and pains is a difficult task. The breadth of the field, the lack of clearly defined disease manifestations and mechanisms, and almost complete lack of leads makes the medical approach difficult. We find that many persons with minor aches and pains sum up their problem by saying that they have not had any fun in years and that they can barely drag themselves around. They have vague joint pains, and perhaps even more difficult to endure is their great fatigue. Because of the vague nature of their complaints, such as "nervousness," "forgetfulness," "I'm all worn out," "aching in my joints and muscles," they often are called neurotics and usually considered nuisances. Most of them have had long-continued treatment of one sort or another which has failed to give them relief and they become frustrated in their search for relief.

Still speaking of minor aches and pains, we know that as we become older we experience a multitude of little maladies, which often persist or disappear only to recur again and again. They constitute no serious threat to life, yet they are annoying and may handicap. Frequently these minor disorders are precursors of more disastrous impairment. In many persons they become the basis of an anxiety state. Most of these anxieties are needless. Muscle cramps, aching of the joints, and innumerable symptoms are experienced by virtually every person at one time or another. The circumstances under which they occur are benign. The same symptoms may appear in association with a wide range of underlying disturbances, some of which are transient while others are ominous. There are many clinical descriptions of odd and localized symptoms, particularly in older persons who have an impoverished blood supply. The disturbance of the underlying mechanisms is not understood. The facts are meager and there is much obscurity surrounding all of them. There is much guessing and much concern about such complaints.

Our group is trying to devise methods for the better management of these problems. We have given temporary and transient relief to hundreds of persons by administering aspirin and, in some instances, steroid and aspirin mixtures, with the result that many of them have resumed much more active function. As a time-honored procedure, patients have rubbed liniments on their afflicted muscles and joints. We chose to study one, Intracel, (topically applied pain killer containing salicylamide benzocaine, and 46% isopropyl alcohol) to

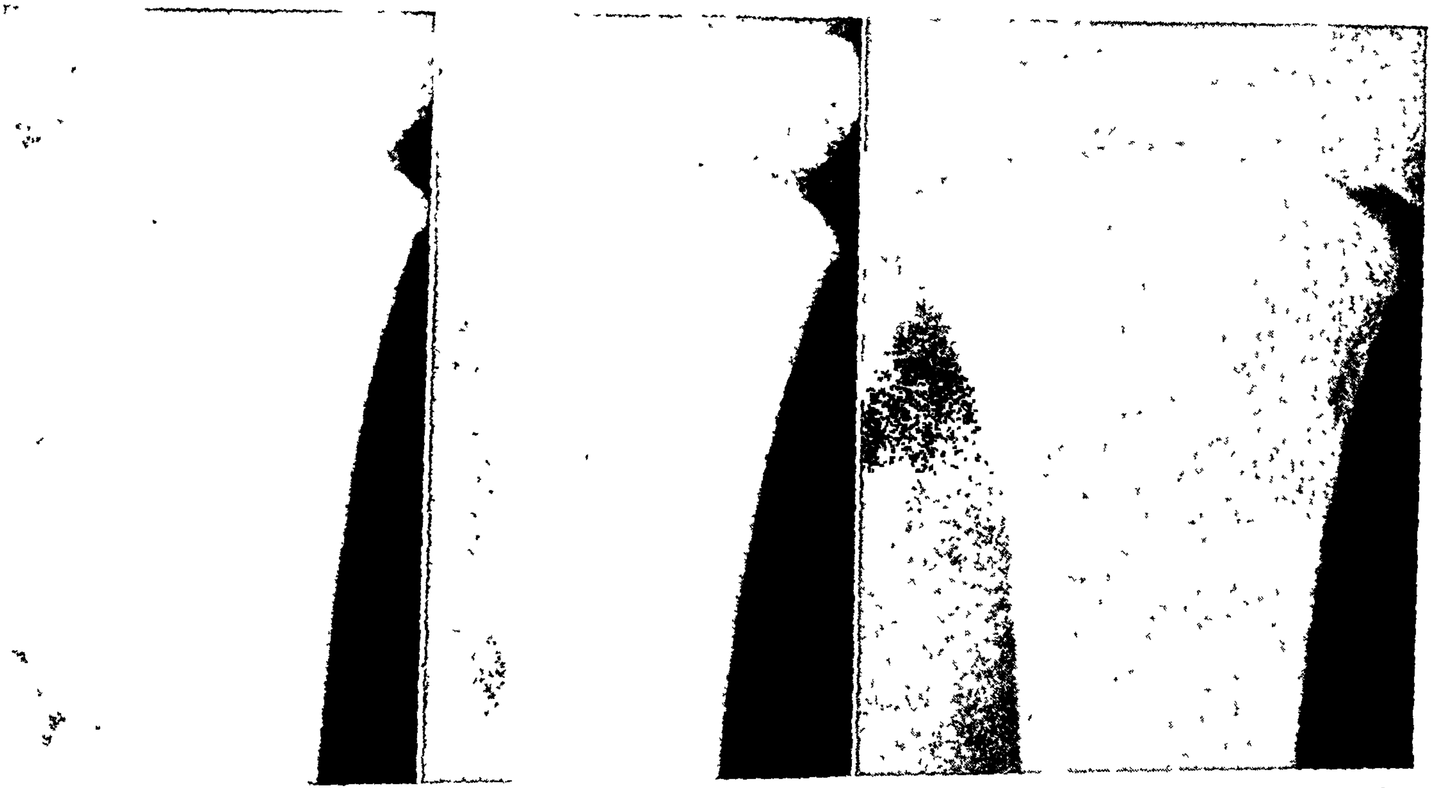


Fig. 19.—*Left*, transverse radiopaque line caused by interference with nutrition of patient in case 9 at time she had typhoid. As bone increased in length, transverse line became farther removed from joint surface (*center*). Eventually, line disappeared (*right*). This is the orderly sequence of events that each such scar goes through.

see if we could work out the mechanism of action. We are still working on it. Many patients think they get relief. After the rubbing of this material on a patient, we have demonstrated that salicylates are excreted into the urine, but we have not been able to show a clear-cut cause and effect relationship between the absorption of the salicylate and the relief of symptoms oftentimes experienced by the patient.[6a] It would seem that better studies of the remedies that patients find helpful should be devised.

For ever so long many physicians have given primary attention to the terminal stages of chronic disease. Yet, it is in the early stages that the physician can do so much. Before we can make great strides, those of us doing investigation will be required to make painstaking biochemical, physiological, and pathological studies that will lead to better diagnostic measures and therapeutic remedies. In the meantime, the practicing physician should be concerned in relieving his patients, in preventing the sequelae, and in keeping them contented and at work. He must treat the patient rather than the disease. Every patient with an anxiety state, disability, or symptom, no matter how "minor," offers a challenge to the physician.

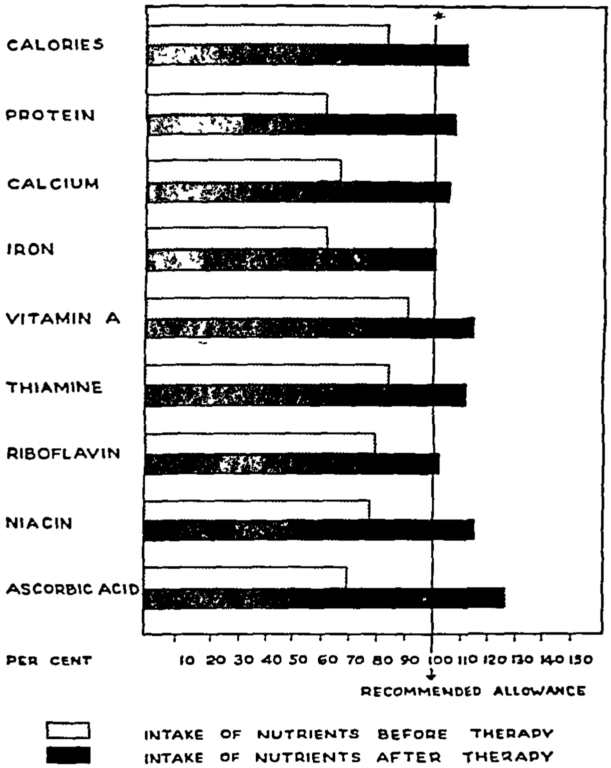


Fig. 20.—Comparative intake of nutrients before and after therapy with prednisolone and aspirin in patient with rheumatoid arthritis. Asterisk indicates allowance recommended by Council on Foods and Nutrition, National Research Council.

Effects of Malnutrition and Undernutrition on Nervous System

We all know that mental illness is a major medical problem. I wish to discuss briefly with you some of the effects of malnutrition and undernutrition on the nervous system. Think of the loss of creativeness and productivity caused by this type of illness alone! Who can estimate its cost in terms of human misery?

In the past, mental illness has been considered a social, moral, or legal problem. To me, the medical profession has the responsibility of treating patients who are mentally diseased, and of preventing mental illness. As physicians, we all know that mental disorders may be an alteration of social behavior, an abnormal emotional response, a neurosis, or a psychosis. The patient may be slightly incapacitated or he may be stricken with a major psychosis that makes hospitalization necessary. It is well to remember that mental disorders are prevalent wherever human beings exist.

Some of the custodial institutions for mental diseases are doing better and better work, but I sometimes wonder if others should not be called "containers of sick people" or "storehouses of sick people." At any rate, the problem is great. Ever since insane asylums have existed, the pellagrin has been pushed into them. These patients were not recognized as pellagrins. Usually the diagnosis was "psychogenic" psychosis. They may have been mistaken for a "schizophrenic," a "manic depressive," or some other classified type of psychosis. Having trained myself more as a nutritionist than as a psychiatrist, I was more impressed by the prolonged dietary deficiency of these patients than by their psychic alteration. Eventually my associates and I found that a lack of niacin in their diets allowed the mental symptoms to arise.[7] After its administration, these symptoms disappeared. Thus we showed that the relief of one particular kind of undernutrition or malnutrition could produce complete relief of mental symptoms. Until this time pellagra was viewed as a mental illness practically incurable. Thanks to the recommendation by the American physician of widespread use of niacin, the disease has practically disappeared.

My associates and I are now in the process of making a 20-year appraisal of niacin as a therapeutic agent. An effect on the second generation is already apparent and can be visualized by means of the following brief case history of a mother and her daughter.

Case 11.—The mother was born in north central Alabama and was of Anglo-Saxon stock. She married a hard-working young man who also was of Anglo-Saxon extraction, and they were in good circumstances until the "depression" closed the coal mines in 1929. The husband said, "When the mine shut down, I was thrown out of work." From that time on the diet consisted of corn bread, "fat back," syrup, and occasionally beans or an egg. The wife began losing body weight, and after the birth of each child she found herself weaker and weaker. In 1933 she began having "pellagracy" each spring. This "breaking out" of the skin appeared on her ankles and forearms and each year it was associated with "nervous crying spells." Her husband said that in 1936 she suddenly "went right out of her mind," and in February of that year she was committed to a mental institution.

Four months after the mother's admission, the abovementioned child was born. It is this child, literally born in a mental hospital, whom I would like to tell you about now. The mother, who was treated with niacin and a better diet, took this child home, and at an early age this child did some of the housework and, when two younger children were born, helped with them. In time she went to high school, where she was an excellent student, and her teacher stated, "She is talented and very responsible." She graduated from high school and also graduated from the university, where she won a number of competitive scholarships.

Comment.—In summary, certainly the mother could not have been released from the institution without treatment, and it is doubtful that she could have worked hard and continued to have children if she had not had treatment from time to time in her home. But, even more impressive to me is the fact that a baby born in a mental institution was able, through the efforts of her mother and, later, of herself, to win competitive scholarships.

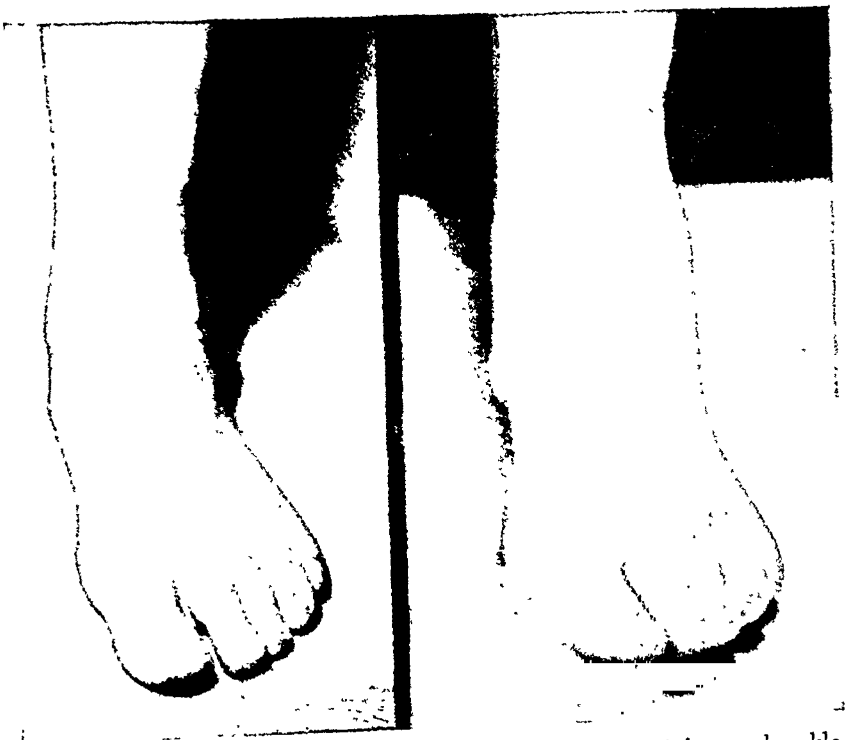


Fig. 21 (case 10).—*Right*, swelling of lower part of leg and ankle before treatment; *left*, same leg after four days of therapy.

The older physicians among you, of course, are well acquainted with the severe mental symptoms of pellagra that manifest themselves in various types of psychoses. Perhaps the most common is that in which loss of memory, disorientation, confusion, and confabulation are predominant. In some types excitement, mania, depression, and delirium predominate. In our experience a paranoid condition is common in pellagrins. These patients, acting on their paranoid delusions, are more active than other pellagrins with psychoses.

After we had learned how to correct the baffling brain changes associated with the severe mental illness of pellagra, we began to grapple with the problem of how to relieve people who had early symptoms only. Soon we learned that many persons who had prolonged dietary deprivation suffered from what was called "hysteria," "anxiety," "extreme nervousness," or "depression." These people disliked bright lights, bright colors, noises, odors once tolerated, and foods once relished. They described themselves as being "jittery," "nervous," "restless," "fractious," and "tense." They stated that they constantly expected something terrible to happen. Still others complained of a poor memory, a memory so poor that they could not remember even what happened 10 minutes before. The patients with the milder afflictions tended to become worse as time went on, and many of them developed personality disorganization.

It is not my intention to delve deeply into why these people could not satisfy their longing for inward peace. I could not accept the concept that their brains were irreparably damaged; it seemed that the cells were waiting listlessly and would function again at full efficiency when we gave them the required nutrients. To make a long story short, we showed that not only niacin was necessary for the integrity of the nervous system but thiamine too. In samples of blood entering and leaving the brain, my associates and I observed a profound alteration in the content of glucose and lactic acid. By studying the oxygen utilization and the lactic acid production, we learned that in patients with vitamin B_1 deficiency and with mental symptoms, the cerebral metabolism was diminished by 60%.[8] These observations afforded a basis for the explanation of our clinical demonstration that thiamine relieved the mental symptoms in a syndrome complex which we termed the initial nervous syndrome. This syndrome can now be prevented with administration of thiamine and niacin. Other vitamins, such as pyridoxine, folic acid, and vitamin B_{12} under certain circumstances may be useful in correcting symptoms arising from the nervous system. Today it is with prevention that you and I, as physicians, are primarily concerned.

Our group long ago learned that the emotional disorders of older people can sometimes be overcome or relieved through the science of nutrition. So many of the older patients have an initial complaint of mental fatigue. They learn that by renewed effort they can adjust, but the process of decompensation worries them and anxieties and depression may develop. They feel they are no longer needed, and many of these people have no incentive for living. They resist changes and their habits become fixed. In many the personality becomes disorganized or rigid and the judgment poor. They lose insight and accept flattery hungrily. Some of them let reality slip away. All too often they confuse manliness and sexual ability. They may develop insomnia and later may become disoriented as to time, place, and, finally, person. It is in this manner that aging brings to them accumulated emotional trauma. All too often the patients have a diagnosis of cerebral arteriosclerosis with psychosis, using age as the only criterion. In trying to aid these people, we assume that their personality is the result of their hereditary factors and their experiences, and that their incapacitation, whether due to a mild neurotic disorder or to a major psychosis, is not necessarily irreversible. Whatever their permanent cerebral incapacity may be remains to be established, but the physician must not accept it without trying to do something for the patient.[6a]

Whether among the old or the young, symptoms arise from damaged tissues. In general, we stress that the processes of protection or of repair will be impeded in tissues that are nutritionally deficient. Mere duration of life is not enough. From time to time we have given you examples of the cells being damaged but not being finished. Give them what they need and they will muster strength and come back. We do not have enough information, of course, to know all they need. The science of nutrition has only scratched the surface, but it has made some progress toward a real solution of mental illnesses.

We know that many nutrients are necessary for the integrity of the nervous system. Yet many persons with anxiety and tension states do not have their neuroses relieved by application of any or all of the nutrients now known. Accordingly, it seemed imperative that we study the so-called tranquilizers or ataractic drugs from the viewpoint of their effect on nutrition. This study is still under way, but we can say that there is, under certain circumstances, a loss of nutrients when these drugs are used and that the safest and best way of using them generally is to be certain that there is a platform of solid nutritional therapy instituted to protect the nervous system. The tranquilizing drugs certainly are an effective aid in managing severely disturbed, hospitalized psychotics, but special attention should be given to the nutrition of these patients because some of them can be helped by nutritive methods. In the past 20 years we have relieved many persons of symptoms arising from the nervous system with synthetic vitamins and a good diet. Yet these persons had no clinical evidence on which a definite diagnosis of deficiency disease could be made. On several occasions I have talked with Dr. John T. Ferguson, who is studying this aspect intensively, particularly in older people. It occurred to me that in our clinic we could be of most service in working with the milder afflictions.

The great majority of people with nutritive failure and "functional" mental disorders respond promptly and completely to adequate nutritional therapy, but there are some who have anxiety states that cannot be corrected entirely by nutritive therapy alone and it is with those people that this particular study is concerned. Conversely, some "functional" mental symptoms arising from nutritive disorders are not corrected adequately by giving the tranquilizers alone—that is to say, vitamin therapy does not replace tranquilizers and tranquilizers do not replace vitamin therapy, but, when indicated, they should be used properly together for the benefit of the patient. Obviously we could not study all the tranquilizers so we chose meprobamate (Miltown, Equanil) because it is well tolerated, orally effective, and suited for prolonged therapy. The following brief case history is illustrative of what can be done by the judicious use of vitamin therapy and a mild tranquilizer.

CASE 12.—A 49-year-old white man was first brought to the Nutrition Clinic of the Hillman Hospital in 1940 complaining of weakness, weight loss, photophobia, soreness of the mouth and tongue, pain and burning of the legs and feet, forgetfulness, and depression. Physical examination showed a man with nutritive failure. He had pellagrous glossitis, great dilatation of the conjunctival vessels associated with photophobia and lacrimation, excruciating tenderness in the nerve trunks of his legs, and hyperactive Achilles and patellar reflexes. His diet for many years was composed chiefly of refined carbohydrates and fats. He rarely ate protein in the form of meat, milk, or eggs. In a period of some 10 years he lost 25 lb. (11.3 kg.) in body weight. He was worse in the spring and fall of the year, and, although his course was not steadily downhill, his symptoms were somewhat more severe with each recurrence. Because of the severe pain in his feet and legs and his sleeplessness, he was given an injection of thiamine. Within six hours the pain had disappeared and that night he slept better than he had for a long time. We then decided to give him sterile saline solution as a placebo. The pain in his feet and legs returned within 48 hours and it was not relieved by saline solution. Without his knowledge the saline solution was replaced with thiamine, 10 mg. parenterally twice a day for a week. Again the pain was promptly relieved and he was able to sleep. For the following month he was given by mouth 10 mg. of thiamine daily and 50 mg. of niacin 10 times a day. Within 48 hours after this therapy was started his pellagrous glossitis disappeared, his appetite increased, and his forgetfulness and depression were relieved. The symptoms arising from his eyes were not relieved, and we decided to give him injections of riboflavin, 10 mg. twice a day for a week. The dilatation of the conjunctival vessels, the lacrimation, and the photophobia began to decrease on the second day of therapy, and by the seventh day the eye symptoms were greatly relieved. This patient's diet improved, but it has not always been completely adequate and he has required treatment from time to time. In the fall of 1957 he had influenza, and since then has complained of sleeplessness and a "sick stomach." Thiamine or niacin gave him no relief. It was decided to give him meprobamate, 200 mg. every 12 hours. After five days he volunteered that he was sleeping much better, and he no longer complained of having a "sick stomach." In the two months that he has been on this therapy he has had no recurrence of these symptoms.

It is important, as can be seen by this case history, to realize that the mere fact a person has nutritional deficiency does not mean that he cannot have other types of disorders also.

Summary and Conclusions

I have discussed with you a few of the many advances which have been made in nutrition in recent years. You have seen that what patients eat has much to do with their health and with their recovery from ill health. Primary or secondary nutritional disorders produce or complicate all the problems of the sick. I have stressed that we should be concerned with the prevention and with the earlier stages of disease when the disturbances are almost imperceptible and that we should not wait until these disturbances bring tremendous burdens and stark tragedies.

In the beginning man's main concern was the obtaining of food. He did not know that bodily functions are impaired when the cells and tissues of the body are deprived of essential nutrients. Of necessity, our ancestors had to obtain all their vitamins and essential nutrients as they were produced by nature. We have learned that, when fruits, vegetables, eggs, milk, fish, meat, and other foods are not available in adequate amounts, or for any reason are not satisfactory, we must recommend methods of maintaining tissue integrity. We have shown how this may be done by supplementing what foods are available with certain synthetics and food concentrates. This means that the goal we are seeking is to devise methods of achieving biochemical independence for people. To do this, we know that excellent nutrition is basic, that disease is chemical in its origin, that the body cells can fight back to an amazing degree, and that our tissues, when properly replenished, can come into their own again. A number of examples are reported of how this works in actual practice. Above all, we must realize that, as physicians, we are properly the guardians of the health and nutrition of our patients, and it is for us to prevent or treat disease so as to increase their vigor, strength, and happiness.

The studies in nutrition were done at the Nutrition Clinic, Hillman Hospital, Birmingham, Ala., at the Department of Nutrition and Metabolism, Northwestern University Medical School, Chicago, at the Hospital Mimiya, Santurce, Puerto Rico, and at the General Calixto García Hospital, Havana, Cuba.

This paper is based to a considerable degree on concrete data obtained by the associates of the author working in Alabama, Illinois, Cuba, and Puerto Rico.

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SYDENHAM'S CHOREA.—Data . . . suggest that Sydenham's chorea cannot be viewed simply as an organic disease caused by the various long-term consequences of the invasion of the child by bacteria. The evidence, totally considered, suggests rather that Sydenham's chorea is a much more complex disorder, and there is serious doubt that rheumatic fever plays a role in many patients with this illness. Other agents must be sought to explain this illness, and we feel that emotional and interpersonal factors are a promising avenue of such investigation.—A. H. Chapman, M.D.; Loraine Pilkey, M.A.; and M. J. Gibbons, M.S.S.W., A Psychosomatic Study of Eight Children with Sydenham's Chorea, *Pediatrics*, April, 1958.

ECHO-9 VIRUS EXANTHEMA

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and
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A morbilliform rash lasting from one to three days became epidemic in Minnesota in 1957. It occurred alone or in various combinations with fever and aseptic meningitis; the meningitis also occurred alone in six patients. Each strain of virus isolated from patients was identified by appropriate neutralization tests, and acute and convalescent phase human serums were assayed for neutralizing antibodies. The pathogen was thus found to be a strain of the enteric cytopathogenic human orphan virus ECHO-9. It resembled the prototype ECHO-9 in its behavior in cultures of cells from monkey kidney, human amnion, and the HeLa strain of human carcinoma, but it possessed the additional properties of pathogenicity for newborn mice and for tissue cultures of human foreskin cells. In its pathogenicity for newborn mice it resembled certain European, English, and Canadian strains of ECHO-9. This virus is believed to have caused as many as 400,000 infections in the whole state.

Exanthema caused by ECHO-9 virus, a recently recognized disease entity, must be differentiated clinically from other short-term exanthemas such as rubella, Boston exanthem,[1] and roseola infantum. Recognition of ECHO-9 virus in 1953 resulted from inoculation of monkey-kidney-cell cultures with material taken as a rectal swab from a healthy child in Ohio.[2] Known epidemics of ECHO-9-virus–induced aseptic meningitis occurred in Europe[3] and England[4] in 1955 and in 1956 and in Canada[5] in 1956. The epidemic syndrome was predominantly aseptic meningitis, although skin rash was seen in some patients.

During the summer of 1957 an epidemic of exanthema occurred in Minnesota. In summary of clinical details,[6] it can be stated that the patients presented a generalized morbilliform rash lasting one to three days. Some patients showed fever. Commonly, infection spread within families and within neighborhoods. While rash alone was common, symptoms of all patients made up a spectrum ranging from inapparent infection to skin rash with little disability, skin rash and fever, skin rash and aseptic meningitis, and, finally, aseptic meningitis without rash.

This article describes laboratory data establishing an etiological relationship between ECHO-9 virus and the epidemic exanthema seen in Minnesota during 1957. Two properties of the Minnesota strain of ECHO-9 virus are noteworthy: (*a*) pathogenicity for suckling mice in contrast to lack of such pathogenicity of the prototype ECHO-9 virus[2] and (*b*) pathogenicity for human foreskin cells in tissue culture.

(The incidence of disease from ECHO-9 virus in Minnesota during the summer of 1957 was estimated by the Minnesota Department of Health in a bulletin distributed to all physicians on Oct. 14, 1957. Instances of aseptic meningitis with or without exanthema were determined by canvass of 400 households randomly selected in the Minneapolis–St. Paul area. Projection from survey findings suggested that over 200,000 cases of ECHO-9 virus infection occurred during the summer of 1957 in the Minneapolis–St. Paul areas of Minnesota and that as many as 400,000 cases occurred in the whole state.)

Laboratory Methods

Specimens.—Stool specimens were frozen at –70 C in screw-capped glass jars within 12 to 24 hours after collection. Within a week, the feces were suspended to an approximate concentration of 20 Gm. per 100 ml. of glass-distilled water containing 0.001% phenol red. Supernatant fluid was harvested after centrifugation of specimens at 18,400 g for 30 minutes at 3 C; 200 units of penicillin and 100 mcg. of streptomycin (standard concentrations for this laboratory) were added per milliliter of fluid. These fluids, in sealed glass ampuls, were stored at –70 C for from days to weeks before inoculation into cell cultures or mice.

Throat swabs were immersed in 3 to 4 ml. of nutrient broth immediately after collection. Thereafter, the broth was centrifuged and stored as described above. Serum specimens representative of acute and convalescent phases of disease were stored at –20 C.

Preparation of Cell Cultures.—Primary cell cultures of cynomolgus and rhesus monkey kidney and of human amnion and cultures of HeLa cells were prepared as described.[7] For virus isolation or neu-

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tralization tests, monkey kidney cells in 16-by-125-mm. tubes were maintained under 0.8 ml. of Hanks' balanced salt solution (BSS) containing 2% calf serum, 0.5% lactalbumin hydrolysate, and antibiotics. Similar cultures of HeLa and human amnion cells were washed thrice with one milliliter of BSS and maintained under 0.8 ml. of BSS containing 10% calf serum, 0.1% Difco Yeastolate, and antibiotics.

Human foreskin tissue was cut with scalpels into pieces approximately 1 mm. in diameter, embedded on coverslips in chicken plasma clotted with chicken embryonic extract, placed in Leighton tubes, and incubated in BSS containing 10% human serum, 0.1% yeast extract, and antibiotics. When at least one explant per culture developed a corona of fibroblast-like cells, each selected culture was rinsed twice with 2 to 3 ml. of BSS and covered with 0.8 ml. BSS containing 10% calf serum, 0.1% yeast extract, and antibiotics. All cultures were grown or maintained for virus tests at 37 C.

Isolation of Virus.—Tube cultures of monkey kidney, HeLa, or human amnion cells were inoculated with 0.1 ml. of undiluted virus specimen and incubated at 37 C. Cells magnified 50 or 100 times were observed for 10 days or, in the case of foreskin cultures, for 21 days. Newborn Swiss albino mice (from litters no older than 48 hours) were concomitantly inoculated intracerebrally with 0.02 ml. and intraperitoneally with 0.05 ml. of virus specimen and observed for 14 days.

Identification of Virus.—Each ECHO-9 virus strain isolated from patients was identified by neutralization test with monkey-kidney-cell cultures. Test virus (75-250 $TCID_{50}$) was incubated with homotypic monkey antiserum containing 20 units of ECHO-9 neutralizing antibody, according to the technique recommended by the committee on ECHO Viruses.[8] Cultures incubated at 37 C were observed for five days. Virus-neutralization tests done with human foreskin cultures or mice as indicators were performed similarly, except that cultures were observed for 21 days and mice for 14 days. Neutralization tests for ECHO-9 virus as 10% mouse-muscle suspensions involved use of 50 units of antibody and concomitant intracerebral inoculation of 0.02 ml. and intraperitoneal inoculation of 0.05 ml. of antibody-virus mixture.

Assay for ECHO-9 Neutralizing Antibody in Serum.—Neutralizing antibodies were titrated with primary monkey-kidney-cell cultures. Test human serums were serially diluted twofold in the maintenance medium specified for kidney cells. Serum dilutions were mixed 1:1 with virus suspension representing 150-500 $TCID_{50}$ per milliliter; mixtures were incubated for one hour at room temperature (22-30 C). Each virus-serum mixture in 1-ml. amount was inoculated into two tube cultures containing only cells attached to glass (no fluid medium). Cultures were incubated at 37 C and observed under the microscope on day 1 or 2 and day 5. Titration end-points represented the highest

TABLE 1.—*Evidence for ECHO-9 Virus Infection in Patients with Exanthem and/or Aseptic Meningitis*

	Patient				Virus Isolated (+) or (0) from					Homotypic Neutralizing Antibody Titer	
Syndrome Class	No.	Age, Yr.	Sex	Onset of Symptoms, Date	Throat Swabs		Stools		Spinal Fluid	Acute Phase Serum	Convalescent Phase Serum
Exanthem only..................	1A*	2.5	M	7/20	+(3)†	...	...	...	CSF not available	<10(3)‡	80(31)
	2	23	F	7/21	+(4)	...	...	...		<10(4)	80(23)
	3	7	M	7/21	+(7)	...	+(11)	0(9)		<10(7)	40(39)
	4A	6	M	7/22	+(1)	...	+(10)	...		<10(3)	80(31)
	5B	2.5	M	7/25	+(4,10)	0(29)	...	...		<10(4)	80(28)
	6C	33	M	7/27	+(4)	...	...	...		<10(4)	40(18)
	7C	35	F	7/27	+(5)	...	...	...		<10(4)	80(24)
	8B	4	M	7/31	+(4)	0(23)	+(6)	...		4(4)	>128(22)
	9	10	F	8/17	+(3)	0(4)	+(8)	0(13)		<10(3)	40(33)
	10	3	F	8/18	...	0(2)	+(3)	...		<10(2)	80(32)
					10/14§	...	5/7§	...		...	...
Exanthem and aseptic meningitis	11	7	F	7/28	...	...	+(9)	0(7,8)	...	<10(7)	80(43)
	12	13	M	7/28	...	...	+(9)	0(7.8)	...	<10(7)	10(18)
	13	14	F	8/ 3	+(6)	...	+(7,11)	...	...	<10(6)	160(34)
	14	9	M	8/ 9	...	...	+(2,4,5)	...	...	<10(3)	80(33)
	15	7	M	8/28	...	...	...	...	...	<10(3)	40(34)
					1/1§	...	7/11§	...	...	...	...
Aseptic meningitis..............	16	11	M	7/17	...	...	+(9,6)	...	+(4)	<10(6)	160(56)
	17A	26	F	7/23	...	...	...	...	...	<10(8)	>640(30)
	18	38	M	7/30	...	...	+(5)	...	+(3)	<10(3)	40(45)
	19B	29	F	7/31	...	...	...	...	...	<10(-795)	80(31)
	20	3.5	M	7/31	...	...	...	...	...	<10(6)	>320(42)
	21	9	F	9/ 3	...	...	...	0(1)	...	<10(1)	40(48)
					...	...	3/4§	...	2/2§	...	...
Fraction of all specimens positive........................					11/15 (0.73)		15/22 (0.68)		2/2 (1.00)	21/21 (1.00)	

* A, etc., designates patients from single families.

† Figure in parenthesis is day of illness when specimen was obtained, counting the first day of symptoms as day 1.

‡ Neutralizing antibody titers are given as highest dilution of serum that completely neutralized 75 to 250 $TCID_{50}$ of ECHO-9 virus from patient 6 when tested in two tube cultures of monkey kidney cells.

§ Fraction of specimens positive.

serum dilution completely preventing cell destruction in both cultures. Antibody assays were accompanied by control titrations of test virus to determine exact virus dosage as TCID$_{50}$. For this purpose, virus was mixed 1:1 with calf-serum medium.

Results

At the beginning of the exanthema epidemic in Minnesota during the summer of 1957, the disease was thought possibly to be Boston exanthem,[1] now classified as infection by ECHO-16 virus or a closely related agent.[9] The Boston exanthem virus was described originally as cytopathogenic for fibroblasts but not epithelial cells.[1] In initiating study of the Minnesota epidemic, tissue cultures of human fibroblasts were therefore used in attempts to recover an etiological agent. Additional inoculation of material from throat swabs and feces into monkey-kidney-cell cultures, however, resulted in prompt recovery of ECHO-9 virus. Because it was then evident that the exanthema involved ECHO-9 virus rather than the agent of Boston exanthem, monkey-kidney-cell cultures were used for the remaining virus isolation tests.

Correlation of Exanthema with Human ECHO-9 Virus Infection.—Fifteen exanthematous patients (table 1) yielded complete series of specimens, including acute and convalescent-phase serums, throat swabs, and/or feces. These patients ranged in age from 2.5 to 35 years; their illnesses began between July 20 and Aug. 28, 1957. Fifteen throat swabs were obtained from 11 patients; 11 swabs from 10 patients yielded ECHO-9 virus upon inoculation into monkey-kidney cultures (table 1). Although most throat swabs yielding virus were taken between the 1st and 5th days of illness, virus was isolated from a swab taken as late as the 10th day of illness. Eighteen fecal specimens were obtained from 9 patients; 12 specimens, representing each of the 9 patients, yielded ECHO-9 virus (table 1). Tests for homotypic ECHO-9 neutralizing antibody were done on serum obtained on days 2 to 7 of illness (acute phase) or days 18 to 39 (convalescent phase). A fourfold or greater increase in antibody titer was found for each of the 15 patients (table 1).

Evidence that ECHO-9 virus did not cause all cases of exanthema occurring in Minnesota during July and August, 1957, is summarized in table 2.

Table 2.—*Instances of Undiagnosed Exanthem Concurrent with ECHO-9 Epidemic of July-August, 1957*

Syndrome Class	Patient No.	Patient Age, Yr	Patient Sex	Onset of Symptoms, Date	Virus Not Isolated (0)* from Throat Swab	Virus Not Isolated (0)* from Stool	Homotypic Neutralizing Antibody Titer Acute Phase Serum	Homotypic Neutralizing Antibody Titer Convalescent Phase Serum
Exanthem ...	22	5	M	7/21	0(9)†	0(8)	10(7)‡	<4(31)
	23	2	F	7/28		0(3)	<4(2)	<4(31)
	24	1	F	7/31	0(5)	0(5)	<4(4)	<4(24)
	25	2	M	8/1	0(1)	0(2)	<4(1)	<4(31)

* Specimens were tested in monkey kidney cells, Hela cells, human amnion cells, foreskin fibroblast explant cultures, and litters of 1-to 2 day old mice inoculated intraperitoneally and intracerebrally

† Figure in parenthesis is day of illness when specimen was obtained, counting the first day of symptoms as day 1

‡ Neutralizing antibody titers are given as highest dilution of serum that completely neutralized 75 to 250 TCD50 of ECHO 9 virus from patient no. 6 (table 1) when tested in cultures of monkey kidney cells These results were confirmed by repeated tests

Table 3.—*Pathogenicity of ECHO-9 Viruses for Cultivated Foreskin Fibroblasts and for Newborn Mice; Comparison of Viruses in Patients' Specimens with Viruses Passed Once in Monkey-Kidney Culture*

Patient No	Syndrome	ECHO 9 Virus Isolated from	Fraction of Indicator Hosts Exhibiting Pathogenic Effect: Foreskin Fibroblasts (Cytopathogenicity) Specimen	Foreskin Fibroblasts (Cytopathogenicity) First Passage	1-to 2 Day-Old Mice Injected Intracerebrally and Intraperitoneally (Paralysis) Specimen	1-to 2 Day-Old Mice (Paralysis) First Passage
2	Exanthem	Throat swab (4)*	0/3†	3/3‡	0/8 0/8†	0/9 0/10
3	Exanthem	Throat swab (7)	1/3§	3/3	0/9 0/11	8/9 5/7‖
		Stool (11)	0/3	3/3	0/7 0/7	0/6 2/13
4	Exanthem	Throat swab (1)	0/3	3/3	0/8 0/8	0/5 0/7
5	Exanthem	Throat swab (4)	0/3	3/3	0/5 0/8	0/8 2/12
6	Exanthem	Throat swab (4)	2/3	3/3	0/10 0/8	6/6 7/7
9	Exanthem	Throat swab (3)	0/3	3/3	0/7 0/7	8/8 6/6
		Stool (8)	0/3	3/3	0/6 0/6	2/10 3/7
10	Exanthem	Stool (3)	0/3	3/3	0/10 0/7	1/9 4/6
11	Exanthem & Aseptic Meningitis	Stool (3)	0/3	3/3	0/10 0/7	2/10 3/7
16	Aseptic Meningitis	Spinal fluid (2)	2/3	3/3	5/12 0/7	6/9
19	Aseptic Meningitis	Stool (4)	0/3	3/3	0/12 0/10	0/5 0/6
		Spinal fluid (2)	0/3	3/3	0/8 0/7	0/6 7/8
Fraction of specimens pathogenic			3/13	13/13	1/13	10/13
			(0 23)	(1 00)	(0 08)	(0 77)
Fraction of virus strains pathogenic			3/10	10/10	1/10	8/10
			(0 30)	(1 00)	(0 10)	(0 80)

* Figure in parenthesis is day of illness when specimen was obtained, counting the first day of symptoms as day 1

† Numerator signifies the number of fibroblast cultures that showed cell destruction, or number of mice paralyzed The denominator indicates the number of cultures inoculated or number of mice per litter For mice, each fraction represents one litter Positive results are shown in bold-face type

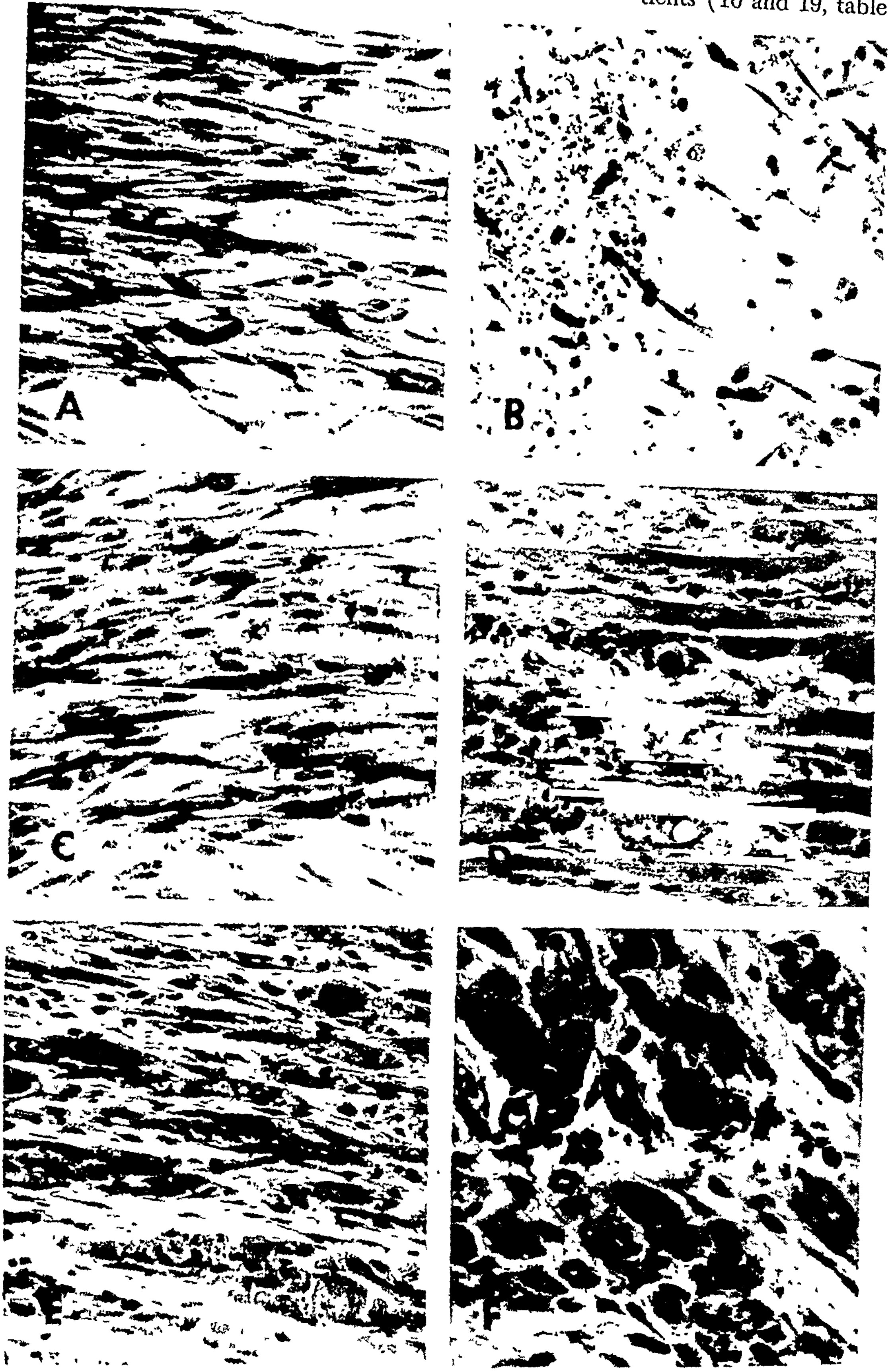
‡ Each virus from first-passage fibroblast cultures inoculated with ECHO 9 strains that were originally isolated in monkey-kidney cultures was neutralized by ECHO 9 monkey antiserum upon second passage in fibroblasts and in monkey kidney cells

§ Each virus from first-passage fibroblast cultures inoculated with specimens from patients 3, 6, and 16 was neutralized by ECHO 9 monkey antiserum upon second passage in fibroblasts and in monkey-kidney cells

‖ Each virus from first-passage mice (as suspensions of hind limb muscle) was neutralized by ECHO 9 monkey antiserum in 1-to 2-day-old mice (inoculated IC and IP) and in monkey-kidney-cell cultures

Four patients, from 1 to 5 years of age, developed skin rash between July 21 and Aug. 1. However, ECHO-9 virus was not recovered from throat swabs or stool specimens, and neutralizing serum antibodies did not appear in significant concentration or increasing titer. Specimens were examined for virus by inoculation of monkey kidney, human foreskin, human amnion, and HeLa cultures and of newborn mice. The fact that the clinical manifestations of disease in these four patients were indistinguishable from illnesses established for other patients as ECHO-9 virus infection emphasizes need for laboratory confirmation of clinical diagnoses of ECHO-9 virus exanthema and/or aseptic meningitis.

Correlation of Aseptic Meningitis with Human ECHO-9 Virus Infection.—Five of the 15 patients with exanthema suffered aseptic meningitis; 6 other patients exhibited evidence only of aseptic meningitis (table 1). Serum neutralizing antibody titers for all patients rose during convalescence, and ECHO-9 virus was recovered from feces and/or throat swabs. Cerebrospinal fluid obtained from two patients (16 and 19, table 1) on the fourth and third respective day of illness yielded ECHO-9 virus. This laboratory evidence supported the conclusion that ECHO-9 virus has caused aseptic meningitis in these patients.



A, B, and *C,* foreskin fibroblasts stained with hematoxylin and phloxin (magnification 100×). *A,* normal fibroblasts. *B,* remnants of fibroblasts destroyed six days after inoculation of ECHO-9 virus as first-passage monkey-kidney harvest from the throat swab patient of 6 (table 1). *C,* normal fibroblasts in a culture seven days after inoculation of the same virus as in *B* and ECHO-9 monkey antiserum. *D* and *E* (magnification 200 ×) and *F* (magnification 400 ×), infant mouse muscle stained with hematoxylin and eosin. Mice were inoculated with first-passage monkey-kidney harvests of ECHO-9 virus from, *D,* patient 6 and, *E,* and *F,* patient 3. Note necrosis of myofibrils, inflammatory cells, and disruption of normal muscle morphology.

Family Infections by ECHO-9 Virus.—Three families were studied. In table 1, patients 1, 4, and 17 represent family A; patients 5, 8, and 19 represent family B; and patients 6 and 7 represent family C. In these families, onset of illness occurred sequentially over a period of several days (table 1); apparently, ECHO-9 virus had either spread rapidly in the families or simultaneously infected several family members who varied in period of incubation. ECHO-9 virus was recovered from two other sick members of family A, children aged 1 and 3, from throat swabs obtained on the third days of illness. A fourth member of family B, a child aged 1, yielded ECHO-9 virus from feces obtained on the fifth day of his illness. However, the fifth member of family B, the father, showed no evidence of infection by ECHO-9 virus by test of serum obtained (*a*) prior to the epidemic and (*b*) about 35 days after onset of disease in other family members. These findings suggested that family infections were common but that it was possible for a family member to escape infection.

Pathogenicity of Minnesota Strain ECHO-9 Virus for Foreskin Cells and for Newborn Mice.—The initial use of human foreskin cell cultures to detect Boston exanthem agent revealed an interesting biological behavior of the ECHO-9 virus responsible for epidemic exanthema in Minnesota during July and August, 1957. Foreskin cultures containing predominantly fibroblasts were inoculated with material from six throat swabs, five stool specimens, and two cerebrospinal fluids obtained from a group of 10 patients made up of 7 with exanthema, 1 with exanthema and aseptic meningitis, and 2 with only aseptic meningitis (table 3). These 13 specimens had yielded 10 strains of ECHO-9 virus upon inoculation into monkey kidney cultures. Yet only 3 of the 10 virus strains (from patients 3, 6, and 16, table 3) caused destruction of foreskin cells. The three viruses isolated in foreskin cultures were identified by neutralization test with ECHO-9 monkey antiserum upon passage in monkey-kidney cultures and again in human foreskin cultures.

After primary passage of the 10 strains of ECHO-9 virus in monkey-kidney cultures, they behaved differently in foreskin cultures. Whereas only 3 original specimens from patients destroyed foreskin fibroblasts, each of the 10 virus strains after passage in monkey-kidney cells produced such destruction (table 3). Parts *A*, *B*, and *C*, in the figure show representative cytologic effects of ECHO-9 virus strains on foreskin fibroblasts and prevention by ECHO-9 antiserum.

While the prototype of ECHO-9 virus is not pathogenic for newborn mice, certain ECHO-9 strains isolated in England,[4b] Europe,[3] and Canada [5] cause paralysis and death of newborn mice. Ten virus strains isolated in Minnesota during 1957 were therefore inoculated both intracerebrally and intraperitoneally into 1-to-2-day-old mice; these strains were the same as those inoculated into foreskin cultures (table 3). One group of test mice from two litters was inoculated with corresponding virus harvested from monkey-kidney cultures. Only one original specimen, cerebrospinal fluid from patient 16, produced disease in newborn mice (table 3). In contrast, 8 of 10 virus strains harvested after primary passage in monkey-kidney cultures affected newborn mice; infection was revealed by extensor paralysis of hind limbs, which characteristically did not culminate in death but gradually became milder, with eventual recovery of the mouse. Histopathology of this acute myositis of mice is shown in parts *D*, *E*, and *F* in the figure. The pathogenicity for mice and monkey-kidney cells of muscle suspensions prepared from sick mice was neutralized by ECHO-9 monkey antiserum.

Comment

The results of these studies established that ECHO-9 virus was the etiological agent of an epidemic of exanthema in Minnesota during summer of 1957. The ECHO-9 disease ranged from mild exanthema to mixtures of exanthema and aseptic meningitis and to moderately severe but nonfatal aseptic meningitis; however in the patients studied, the skin rash predominated. Epidemiologic findings suggested that the disease had been highly communicable, especially in families.

This establishment of an etiological relationship between ECHO-9 virus and exanthema should not lead clinicians to the general conclusion that all summer rashes are caused by ECHO-9 virus. Such a conclusion would not be valid even were an epidemic of ECHO-9 virus-induced disease existent in a community. Evidence against such a conclusion is presented by findings for the four patients (table 2) who suffered skin rash indistinguishable from that caused by ECHO-9 virus but failed to yield laboratory evidence of ECHO-9 virus infection. These patients likewise did not show evidence, in the form of antibody response, of infection by ECHO-16 virus (either identical or closely related to Boston exanthem agent), ECHO-2 or 14 viruses, or Coxsackie A9, B2, or B5 viruses. The last virus was responsible for sporadic cases of aseptic meningitis in 1957 concurrent with epidemic ECHO-9 virus disease and for epidemic aseptic meningitis in 1956.[10]

In comparison with the prototype of ECHO-9 virus, recovered in 1953 from a healthy child in Ohio,[2] Minnesota strains were distinctive in their pathogenicity for newborn mice. In this respect, the Minnesota strains resembled strains recovered in Europe, England, and Canada during 1955 and 1956. The property of mouse pathogenicity of ECHO-9 virus strains is important in consideration of whether the virus should be classified as Coxsackie or ECHO. Further discussion of this point is not relevant to this paper; a recent analysis of the problem may be consulted for additional information.[11]

The striking change in capacity of Minnesota ECHO-9 viruses to produce disease in mice or destroy foreskin fibroblasts in culture apparently conditioned by passage of the viruses in primary monkey-kidney cultures is noteworthy but unexplained. A single passage in monkey-kidney-cell cultures could have produced such change by (*a*) increasing the concentration of virus and/or (*b*) inducing or permitting qualitative change in virus properties; either quantitative or qualitative changes in virus could result in increased pathogenicity for mice and foreskin fibroblasts.

Summary

ECHO-9 virus was identified by tests with cell cultures and infant mice as the etiological agent of an epidemic of exanthema occurring in Minnesota during the summer of 1957. Infection was manifest by a spectrum including morbilliform rash (most common) and/or aseptic meningitis. Minnesota

ECHO-9 strains were cytopathogenic for monkey-kidney epithelium and human foreskin fibroblasts; they differed from the prototype of ECHO-9 virus and resembled European, English, and Canadian strains in their pathogenicity for newborn mice.

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TREATMENT OF PULMONARY INSUFFICIENCY BY TRACHEAL FENESTRATION

PRELIMINARY REPORT

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Tracheal fenestration is an operation to provide a permanent access to the deeper airways. The stoma can be kept open or closed at will. Its use is here proposed as a new method of treatment in advanced pulmonary insufficiency. The four patients whose cases are described were approaching terminal hypoxia as a result of destructive pulmonary disease. Tracheal fenestration made it possible to remove mucopulmonary secretions by aspiration. The patient gradually learns to do this himself. The immediate relief experienced by the patient after aspiration, and the striking change for the better in the course of the disease in these four cases, indicate that the advantages of tracheal fenestration need to be explored further.

In the treatment of patients with pulmonary insufficiency efforts are now directed toward the relief of hypoventilation by means of mechanical ventilators. Since practical experience has shown that mechanical aids to ventilation are operated most efficiently when used in connection with intratracheal tubes, tracheostomy is being increasingly resorted to in "hypoventilation crises."[1] Such tracheostomies are now usually performed as emergency measures and chiefly as adjuncts to the use of mechanical ventilators.

Current procedures, we believe, fall far short of the real goal of treatment of pulmonary insufficiency, and we are accordingly proposing tracheal fenestration as a new method of treatment. When performed at an early phase of pulmonary insufficiency, we have found that it provides an excellent means both of maintaining the airways free of obstructing secretions and of keeping them well ventilated. Elective tracheal fenestration not only obviates the need for mechanical ventilation but also makes possible the prevention of "hypoventilation crises." Such prevention, we feel, should be the goal of treatment in pulmonary insufficiency, the clinical course of which is characterized by a sequence of such crises, which may lead to death by apnea and asphyxia.

In this preliminary report we wish to discuss the following three aspects of this new method of treatment: (1) the need for early and permanent tracheal opening in pulmonary insufficiency, (2) possible accomplishment by elective tracheal fenestration, and (3) mode of action.

Advantage of Preexisting Tracheal Opening

The need for early and permanent tracheal opening in pulmonary insufficiency was impressed upon us through certain clinical observations in patients whose lives were greatly prolonged and made comfortable by means of a preexisting tracheal opening which had been used to great advantage in maintaining open and well-ventilated airways. The following case history will best demonstrate this.

Case 1.—A frail middle-aged woman had extensive confluent tuberculosis involving both her lungs and her larynx. The tuberculosis of the larynx threatened airway obstruction, and the patient required a tracheotomy with cannula at an early phase of the disease. The process resulted in complete destruction of her left lung, with vast honeycombing of giant cavities producing large quantities of pus. In the right lung the disease progressed at a slower rate. She lived to benefit from chemotherapy, which arrested the lesions in the right lung, leaving it in a state of advanced fibrosis and emphysema. Eventually she was left with a pulmonary reserve so low that it barely permitted her more than a bedridden life. The chest x-ray (fig. 1) demonstrates her pulmonary disease at that time.

We observed this invalid patient for 10 years, during which her life depended almost entirely on the skillful maintenance of patent and ventilated airways attained through frequent bronchial intubation and aspiration with the aid of a small bedside suction pump. At first large amounts of secretions, accumulated in the giant cavities of her left lung, had to be eliminated through the tracheostomy cannula. Asphyxia became a constant threat until finally she dared to discard the cannula. This enabled her to rapidly pass a wider catheter through the naked tracheal stoma. Employing a "to and fro" motion and through the use of stronger suction she was enabled to get rid of much viscid mucopus adhering to both the airways and the tubes. Through these manipulations the airways were kept clear most of the day, eventually requiring fewer and fewer "treatments." As her pulmonary reserve diminished and as the secretions became scant she practiced frequent intubations with a few rapid aspirations. These, she explained, relieved her of a feeling of "tightness in the chest," a symptom usually followed by periods of shortness of breath. It became apparent to us that these intubations and aspirations afforded ventilation and probably relieved air trapping in the lung. At this stage the secretions aspirated had changed in character to very scant colorless, sticky, stringy mucus. During this long protracted period of precarious existence this patient had survived several attacks of biliary colic as well as an operation for the removal of a breast cancer carried out while she was under local anesthesia. She died eventually of "intestinal obstruction from metastatic carcinoma."

Case 2.—A male, aged 47, gave a history of chronic pulmonary tuberculosis of 10 years' duration resulting in extensive fibrosis in both upper lobes, more extensive on the right. With a recent flare-up, severe laryngeal tuberculosis developed, threatening airway obstruction, which required tracheostomy with a cannula. Simultaneously there developed widespread extension of tuberculosis throughout both lungs. Although chemotherapy resulted in much clearing of the recent lesions, there remained so much fibrosis and emphysema that the patient's pulmonary reserve became greatly reduced by the time his tuberculosis healed. Due to this fibrosis and emphysema there was persistent dyspnea, aggravated by continued cough and expectoration characteristic of patients with emphysema and bronchiolitis of any origin. The secretions, although moderate in quantity, were very viscid and difficult to raise through the tracheal cannula. Much relief was now obtained by intubation, aspiration, and inhalation of bronchodilators.

This patient, like the one previously described, was soon led to discard the tracheostomy cannula and to practice intubation and aspiration through the naked stoma in the trachea. Here likewise the material aspirated changed to scant, stringy, sticky mucus. This patient also resorted to aspiration of air from his lungs when he felt tightness in the chest, which was usually the premonitor of attacks of dyspnea. These attacks he could prevent by a few rapid aspirations, which he was then able to follow with vigorous inspirations. He practiced this regularly after exertions as well as after long periods of sleep in anticipation of dyspneic attacks which were signaled by the chest tightness. He acquired the habit of testing his breathing for the need of aspiration by periodic hyperventilation exercises, and for a time it appeared that he might become a habitual hyperventilator. Eventually he learned to manage without aspiration for weeks and then months and resorted to it only for short periods during intercurrent respiratory infections occurring about three to four times yearly. These bronchitic periods were cut short by preventing the accumulation of secretions and the aggravation of his emphysema from protracted cough. Observing this patient over a 10-year period convinced us that the benefits derived from the use of his tracheal opening allowed this patient to live in relative comfort

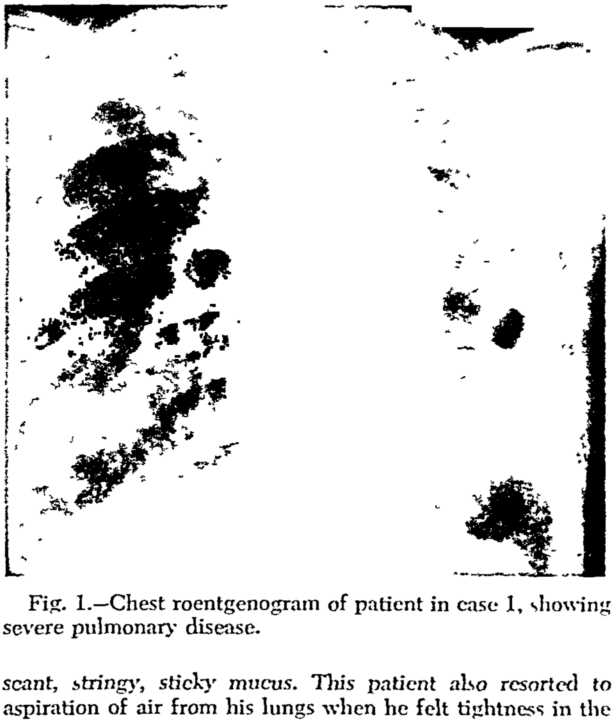

Fig. 1.—Chest roentgenogram of patient in case 1, showing severe pulmonary disease.

despite severe emphysema, extensive pulmonary fibrosis, and marked reduction of pulmonary reserve, as indicated in the x-ray (fig. 2).

In both patients we observed that the creation of a tracheal opening at an early phase of the disease enabled them to prolong their lives greatly despite their low pulmonary reserve. We were able to draw certain significant conclusions: As the pulmonary capacity progressively diminished, these patients became increasingly sensitive to the least interference with ventilation and less tolerant of secretions accumulated in their airways. They increasingly practiced intubation and aspiration to maintain the airways free of secretions. Eventually they aspirated the airways even when little secretion was present. This could serve as a means of creating air currents in their lungs for purposes of ventilation. The early presence of the tracheal opening, enabling these patients to keep their airways clear, has, we believe, prevented added secondary infections, forestalled greater loss of pulmonary capacity, and prevented progression of the emphysema and bronchiolitis in the opposite lung as well as progression to hypoventilation crises so characteristic of advancing pulmonary insufficiency. In view of the irreversible character of the latter, the need for a permanent tracheal opening appears to us obvious. In short, our observations led us to believe that an early as well as a permanent tracheal opening should be a useful means of prolonging the lives of patients with low pulmonary reserve. Accordingly, we began treating such patients by the creation of a permanent tracheal opening.

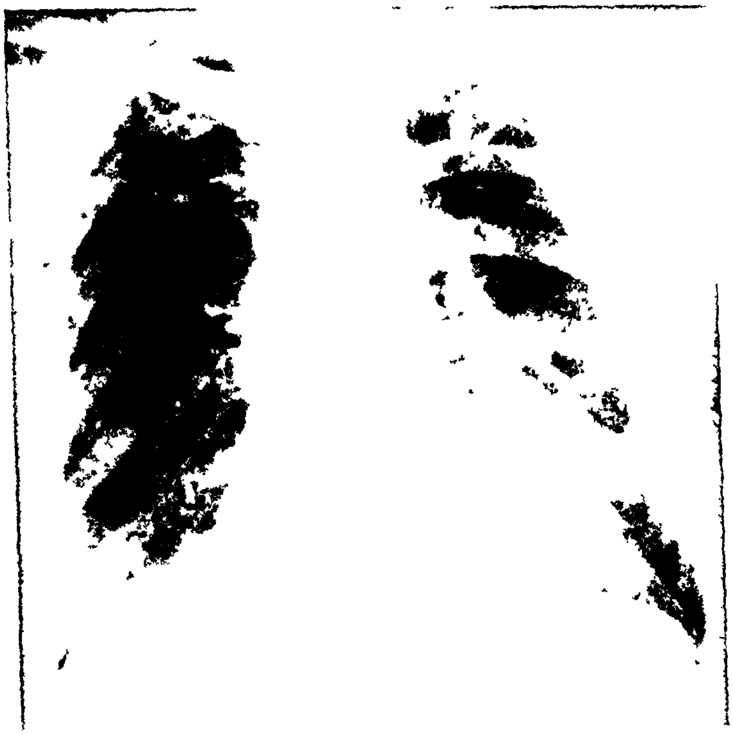
Fig. 2.—Chest roentgenogram of patient in case 2, showing severe emphysema, extensive pulmonary fibrosis, and marked reduction of pulmonary reserve.

Clinical Trials of Tracheal Fenestration

The surgical procedure for creating a permanent window in the trachea which can be kept open or closed at will was worked out by Dr. E. E. Rockey after extensive animal experimentation. This procedure was described by us in recent joint publications.[2] Suffice it to point out here that this also involves a preliminary tracheostomy with cannula through which inhalation and aspiration is practiced for the first few weeks until the tracheal fenestration above it heals and becomes available for permanent use. Two reports follow of patients treated with such fenestration. The operations were performed by Dr. Rockey, who also supervised the subsequent treatment with specially designed bronchial catheters, enabling intubation and aspiration in either side of the chest.

Case 3.—A 52-year-old man gave a history of chronic bronchitis since childhood. However, this condition did not prevent him from playing football for many years, into his late 30's. He dates his illness to postoperative pulmonary complications suffered in 1948, when he was operated on for a double hernia. From that time on, he had suffered from almost constant shortness of breath but with little cough and only scant expectoration. A diagnosis of asthma was given, and he was repeatedly treated accordingly with injections of such drugs as epinephrine. In May, 1956, spontaneous pneumothorax brought him into the hospital in serious condition. He was hospitalized for several weeks. A recurrence of pneumothorax in July, 1956, again confined him to the hospital for several weeks. In August, 1956, he was rehospitalized in a critical condition, and he has remained in the hospital to

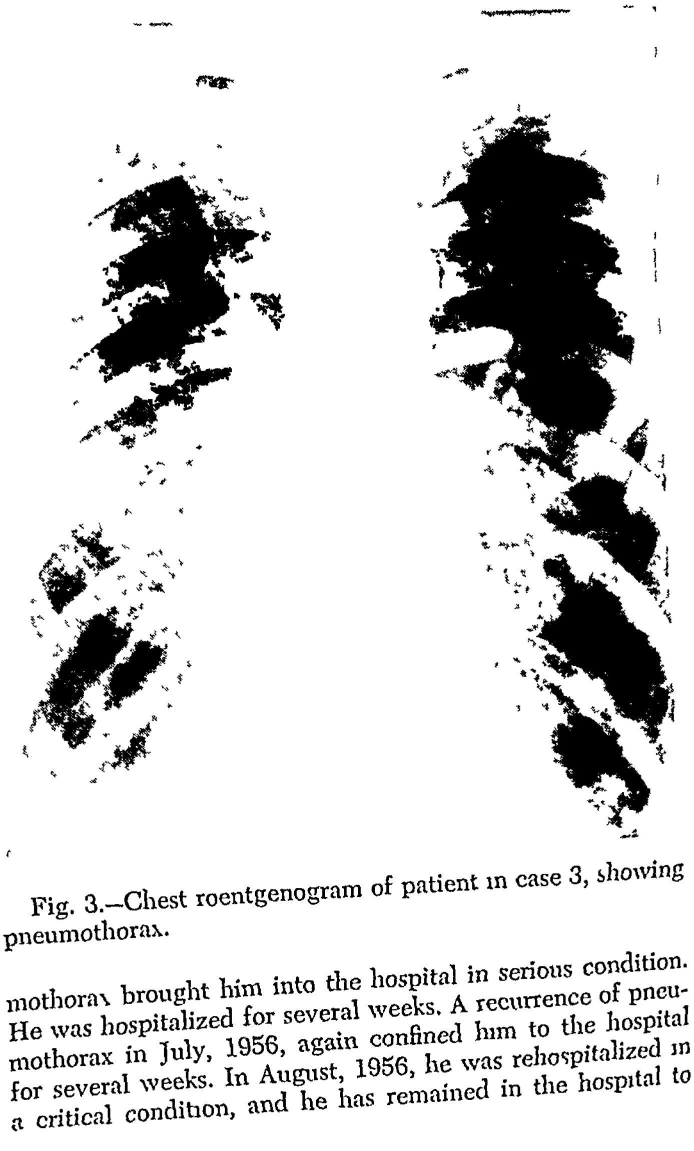
Fig. 3.—Chest roentgenogram of patient in case 3, showing pneumothorax.

the time of writing. The chest x-rays (fig. 3) show the characteristic picture of vanishing lungs with a pneumothorax on the left.

For the first two months in the hospital the patient spent much time in an oxygen tent until his lung reexpanded. After that he continued to suffer from extreme dyspnea. In 1957 he was treated for several severe attacks of aggravated dyspnea but with no pneumothorax. He was treated with steroids, with only temporary response, but with the aid of bronchodilators and oxygen inhalation he was able to continue a precarious existence, barely managing the few steps from bed to bathroom. His exercise tolerance was practically zero, and he was steadily growing weaker and approaching terminal hypoventilation. This was his condition in October, 1957, when he submitted to tracheal fenestration as a last resort. Almost immediately after aspiration of an unexpectedly large amount of mucopurulent secretion his dyspnea was greatly relieved. Five days later he could walk 20 yd. with little shortness of breath, and one week later he could walk twice that distance back and forth. Three weeks after operation he was up and about most of the day and could even ascend a flight of 12 stairs without dyspnea. At first he required frequent aspirations (8 to 10 times daily) and eliminated large amounts of mucopurulent secretions. After a few weeks the amount of secretion diminished greatly (to 4 to 5 cc.), and he required aspiration only three times daily. The patient stated, "I feel like a different man." He slept through the nights without need of aspiration. Three months after operation, he was able to intubate himself with ease whenever he felt the need. By then he was up and about, leading an almost normal life. He now feels fit to resume his previous work.

Case 4.—A 63-year-old man had been suffering from chronic pulmonary tuberculosis since 1950. He had extensive disease involving both lungs, for which he was hospitalized for a period of over two years, from early 1954 until the latter part of 1956. By then much healing of the tuberculous lesions occurred, with extensive fibrosis in both upper lobes, but the sputum was still positive by culture as late as July, 1957. However, with progressive healing of the lesions in his lungs he became increasingly disabled by shortness of breath. In April, 1957, he reentered the hospital chiefly because of persistent dyspnea. The chest x-ray (fig. 4) illustrates the extent of fibrosis and emphysema, which amply accounts for his pulmonary insufficiency at that time. This was greatly aggravated by a severe bronchitis which was present, constantly causing cough with expectoration of about 60 cc. daily. Physical signs corroborated the severe emphysema in both lungs.

Throughout 1957 the patient's general condition deteriorated steadily and he remained hospitalized as a pulmonary cripple, became increasingly bedridden, and required oxygen often for short periods throughout the day. By December, 1957, he could no longer walk the short distance from his bed to the bathroom without experiencing exhausting dyspnea. As a last resort tracheal fenestration was performed in December, and large amounts of mucopus were aspirated both during and after the operation. Almost immediately the urgent dyspnea abated, and he no longer required oxygen. At first the amount of aspirated purulent secretions increased, but soon they decreased and changed to viscid mucus. The breathing improved so remarkably that two weeks after operation he could walk freely about the hospital corridor and even denied dyspnea on mild effort. On Jan. 1, 1958, when the tracheal cannula was removed, he was free of apparent dyspnea, and since then he has been a semiambulant patient. He continues to intubate and aspirate himself about four times daily. He is now fit for light work.

Although in both patients tracheal fenestration was performed recently, we feel justified in presenting this preliminary report, because the immediate results have been so strikingly favorable. We are convinced that these patients will continue to enjoy the benefits from fenestration as did those who were under our observation for many years with their permanent tracheostomy. These results are all the more remarkable since we were not dealing with truly early stages of pulmonary insufficiency. In fact, both patients were practically in critical condition when operated on. In both cases severely disabling and distressing dyspnea was relieved soon after institution of a tracheal opening when efficient intubation and aspiration through the tracheostomy cannula was possible. By the time the fenestration had healed sufficiently for the patients themselves to begin passing the catheter, they were well out of their acute difficulties and easily managed their chronic condition by continuing to intubate and aspirate as the need arose. This merely became a matter of acquiring the desired skill through daily practice.

Fig. 4.—Chest roentgenogram of patient in case 4, showing severe fibrosis and emphysema.

Comment

The question naturally arises as to how tracheal fenestration relieves the symptoms of pulmonary insufficiency. We venture to offer an interpretation. The clinical course of a patient with low pulmonary reserve is characterized by recurrent attacks of what is best described as a "hypoventilation crisis." This may end either in sudden apnea and asphyxia or lead to slowly progressive cor pulmonale and cardiopulmonary failure. Patients who are tided over such attacks may be restored to a "status quo" and continue to live within the limitations of their low pulmonary reserve until the next crisis arises. Mostly, however, each attack further diminishes cardiopulmonary reserve and brings the end nearer. Therefore, only by the prevention of such attacks can life be prolonged.

The evolution of these crises follows a characteristic clinical course which is due we believe to the following sequence of events: The attacks are usually precipitated by a complicating fresh respiratory infection (even a trivial catarrh), by oversedation, by excessive oxygen inhalation, or by a mild bout of congestive failure. Such circumstances generally bring on an increase of bronchial secretion. Failure to promptly eliminate this leads to stagnation, inspissation, and increased viscosity of secretions, resulting in progressive bronchiolar obstruction, increased air-trapping, and diminishing ventilation. The latter becomes further aggravated by persistent cough. All of these bring about progressive carbon dioxide retention, hypoxia, and increasingly labored breathing. Exhaustion in exaggerated breathing effort resulting in hypoventilation closes the vicious cycle, culminating in acidosis followed by congestive failure.

Tracheal fenestration, making possible efficient intubation and aspiration of the airways as often as is necessary, can reverse the above-described process. It relieves obstruction of bronchioles by elimination of secretions and decreases excessive coughing. It may relieve hypoventilation through frequent aspiration of air from the deeper airways, creating sharp expiratory currents which may act to untrap air and deflate air pockets in the lung. Treatment by fenestration can thus break the vicious cycle at any point and quickly bring the hypoventilation crisis to an end. It may also prevent such crises by timely aspirations that can keep the airways patent and ventilated, thereby forestalling provocative events. Obviously treatment must be applied early, before the pulmonary reserve becomes too low.

Clinical observations indicate that when the airways are kept clear and well ventilated, patients may continue to live within the limitations imposed by a low pulmonary reserve even when the latter seems from x-ray appearances to be so low as to make it difficult to believe. The concept of pulmonary reserve is too complex a problem to discuss here. Recently[8] we postulated that this is not merely a matter of apparently available alveolocapillary surface but rather one of bronchioloalevolar structures performing their normal function, acting in correlation with air and blood flow. As yet we know very little about this function of the terminal lung structures, which depends on normal pressures of air and blood flow maintained in the alveoli and in the pulmonary arteriolocapillary bed. Clinical observations have led us to believe that by keeping the airways patent and ventilated, tracheal fenestration enables the functioning lung structures to operate to the limit of their compensatory capacity.

The question will naturally arise as to the omission of blood gas studies and breathing capacity tests on these patients. It should be obvious that the two patients described were in no condition to perform any sort of breathing tests before operation. Furthermore, as their exercise tolerance was practically nil, there seemed to be no need for blood gas analyses. A few weeks after treatment, their exercise tolerance increased so remarkably that again there appeared to be no need for such tests. However, functional studies are now to be made by us on patients operated on in earlier phases of pulmonary insufficiency.

Last but not least in importance are the great advantages of tracheal fenestration in inhalation therapy. Mention was made above of the fact that mechanical ventilators, assistor as well as controller types, are operated more efficiently by way of intratracheal tubes than by way of masks (over the mouth and nose). For this reason tracheostomy is now being resorted to even when these machines are to be used for only short periods of time (days or weeks). In cases when we are dealing with fixed low pulmonary reserve where mechanical ventilatory aids are required for daily treatments permanently (as intermittent positive pressure breathing machines are now used in emphysema), tracheal fenestration obviously offers very great advantages. Similarly inhalation of bronchodilator and of detergent aerosols is far more efficient by the direct way of intratracheal tubes than by way of oral or intranasal insufflation.

The fact will not have escaped attention that, in the cases reported above, although the patients were in rather far-advanced stages of pulmonary insufficiency, no inhalation therapy of any sort was required after tracheal fenestration, and thorough aspiration of bronchial secretions was practiced during and after this procedure. Indeed, the fact that we could so dispense with the use of inhalation therapy as soon as thorough frequent aspiration became feasible is, we believe, further proof of the remarkable efficacy of tracheal fenestration in the management of progressive pulmonary insufficiency.

Summary

We propose tracheal fenestration as a new method of treatment in the management of advanced pulmonary insufficiency. It is a form of therapy that has developed as a result of long-range clinical observations. The following significant facts stand out: As pulmonary reserve diminishes patients become increasingly sensitive to the least interference with the patency and free flow of air in the airways of their lungs. With progression of pulmonary insufficiency, there arises the need for an early and permanent tracheal opening which per-

mits intubation and aspiration of the deeper airways as often as necessary. Intubation and aspiration of the deeper airways as required in the individual case is an effective method of relieving hypoventilation crises. Furthermore it appears to be the best method of preventing such crises in progressive pulmonary insufficiency.

Tracheal fenestration provides a permanent access to the deeper airways, which can be kept open or closed at will. Tracheal fenestration has so far been performed in too few cases and the clinical observations are still too recent for a final statement to be made. However, we believe this preliminary report is justified by the strikingly favorable results obtained.

Addendum

To date Dr. E. E. Rockey has performed tracheal fenestration on four additional patients with emphysema under practically the same conditions. The immediate relief from symptoms was equally striking, and the clinical results so far have been uniformly favorable.

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DIFFUSE GLOMERULONEPHRITIS AS A COMPLICATION OF SUBACUTE BACTERIAL ENDOCARDITIS

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A patient with a long history of abdominal surgery and recurrent fevers finally exhibited gross hematuria, oliguria, nitrogen retention, and other symptoms and signs of uremia. Before death a loud pericardial rub was noted and a severe melena appeared. Significant findings at autopsy were limited to the heart, kidneys, and cecum; the diagnoses were subacute vegetative endocarditis superimposed on an old rheumatic valvulitis, petechiasis of the cecum, and subacute diffuse glomerulonephritis. Diffuse glomerulonephritis is relatively infrequent as a complication of subacute bacterial endocarditis.

Diffuse proliferative glomerulonephritis is an unusual complication of subacute bacterial endocarditis. In an analysis of 52 proved cases of subacute bacterial endocarditis, Newman and coworkers[1] found only one case of diffuse glomerulonephritis, although 8 cases showed evidence of renal insufficiency. Baehr[2] reported 9 cases of diffuse glomerulonephritis in 77 cases of subacute bacterial endocarditis.

It is the purpose of this paper to present a case of subacute bacterial endocarditis in which diffuse proliferative glomerulonephritis, terminating in uremia, occurred. Of note is the fact that blood cultures, including anaerobic studies and bone marrow and postmortem left ventricular aspiration, were all sterile.

Report of a Case

A 58-year-old female entered St. Vincent's Hospital on Feb. 2, 1957, complaining of low abdominal cramps, burning on urination, left flank pain, and fever of two months' duration. The patient had been in relatively good health until Dec. 5, 1956, when shaking, chills, and fever developed 10 days after a sore throat. Under a short course of penicillin therapy, the patient's throat infection had cleared, but eight days later, fever (104 F [40 C]) and nausea occurred, and the patient was admitted to the hospital.

The patient had been followed by one of us (R. J. B.) since 1948, at which time a loud harsh systolic murmur, heard best along the left sternal border, was noted. The patient volunteered, at that time, that she had had "a

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Dr. Robert Hellg Library
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murmur all of her life." There was no history of rheumatic fever. Chest x-rays showed normal cardiac dimensions. Electrocardiograms revealed no abnormalities and numerous urinalyses and complete blood cell counts were normal except for a slight to moderate anemia with hemoglobin level of 9 to 12 Gm. per 100 cc. The patient had undergone numerous surgical procedures between 1923 and 1940, including appendectomy, hemorrhoidectomy, cholecystectomy, hysterectomy (fibroid uterus), intestinal obstruction due to abdominal adhesions, and repair of umbilical hernia.

On admission in December, 1956, the patient appeared thin and had a temperature of 101.2 F (38.4 C). The blood pressure level was 120/80 mm. Hg, pulse rate was 112 per minute and regular, and a grade 3 apical systolic murmur was heard. There was no cardiomegaly. Abdominal examination showed left costovertebral angle tenderness. X-ray examination of the chest was unrevealing. Electrocardiography was normal, except for prominent, peaked P waves in leads 2, 3, and aVF. Urinalysis showed 2 + albuminuria, 1 to 2 red blood cells and 4 to 5 white blood cells per high-power field. There were no casts. The blood urea nitrogen level was 19 mg. per 100 cc. Urine culture grew out colon-aerogens and Proteus organisms sensitive to chloramphenicol. Three blood cultures were negative. The patient was given chloramphenicol, 250 mg. four times a day by the oral route, became afebrile and asymptomatic, and was discharged on Dec. 19, 1956, the 15th hospital day. However, 10 days later, the patient was readmitted to the hospital with a return of fever and left flank pain. Physical findings were identical to the first hospital visit. Intravenous pyelography revealed a bifid right renal pelvis with partial reduplication of the right intrarenal elements. Cystography and retrograde pyelography disclosed a trigonitis and were suggestive of a right pyelonephritis. Urinalyses were normal, but urine culture showed vast numbers of Proteus organisms. A blood culture was sterile. Chloramphenicol therapy was reinstituted, with gradual response. The patient was discharged 20 days later, Jan. 19, 1957, after sterile urine cultures were obtained.

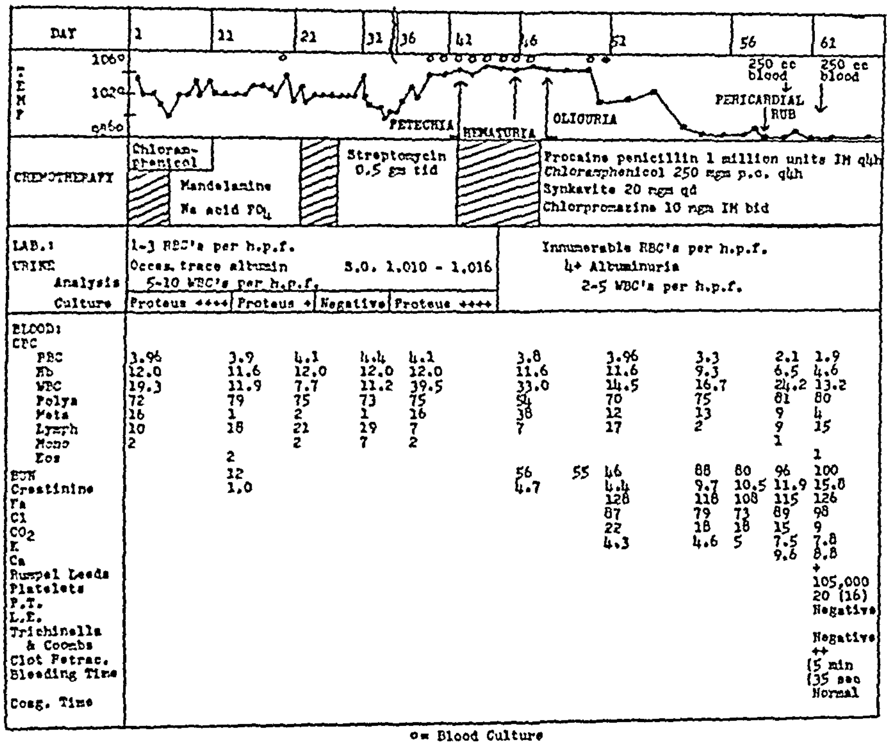

Fig. 1.—Clinical course and laboratory data during patient's final admission.

The final admission occurred on Feb. 2, 1957, because of exacerbation of her previous symptomatology. Physical examination was unchanged. The patient maintained a febrile course (101-103 F [38.3-39.4 C] daily) despite therapy with chloramphenicol and methenamine mandelate (Mandelamine). Daily urinalyses were essentially negative except for persistent finding of 1-3 red blood cells per high-power field and an occasional trace of albumin. On cystoscopy, cultures from both ureters grew out Pseudomonas aeroginosa (in considerable numbers from the left ureter), sensitive only to polymyxin and streptomycin. Accordingly, on the 30th hospital day, streptomycin, 0.5 Gm. intramuscularly three times a day, was instituted, with an immediate response. Nine days later, the temperature rose to 103.4 F (39.7 C) accompanied by shaking chills and, for the first time, petechiae were noted on the left lower eyelid and right buccal mucosa. On several subsequent occasions, small numbers of petechiae developed on the soft pharynx, buccal mucosa, and palpebral conjunctivae. The temperature continued to "spike" daily, ranging to 103-106 F (39.4-41 C). During this time, 15 blood cultures including anaerobic and bone marrow cultures were sterile.

On the 45th hospital day, gross hematuria and oliguria (150 cc. to 600 cc. of urine daily) began and persisted for the remainder of her course. The blood urea nitrogen level rose to 56 to 100 mg. per 100 cc., with an accompanying creatinuria of 4.7 to 15.8 mg. per 100 cc. On vigorous antibiotic therapy, consisting of penicillin, one million units intramuscularly every four hours, and chloramphenicol, 250 mg. every four hours, the patient gradually became and remained afebrile. The clinical picture of uremia supervened and a loud pericardial friction rub was noted six days prior to her death. The blood and pulse pressures rose to 150/60 mm. Hg and remained at that level. Terminally, melena and severe anemia developed, and after a large amount of tarry liquid material was passed by rectum, the patient died.

During the final two weeks, severe left upper quadrant tenderness had developed. However, there was no palpable spleen. No definite alteration in heart murmurs was noted during her hospital course; nor did Roth's spots or Janeway's spots appear. Figure 1 outlines the hospital course during her final admission.

Autopsy Findings.—Autopsy findings of significance were limited to the heart, kidneys, and cecum. The heart weighed 280 Gm. There were many fine filamentous bands between the pericardium and epicardium. The latter was roughened. The mitral valve measured 9 cm. in circumference. The leaflets were rolled and thickened and the chordae tendineae were short and thick. The papillary musculature was hypertrophied. On the posterior leaflet of the mitral valve, at the lateral junction of the posterior and anterior leaflet, was found a firmly attached 0.5-by-0.6-cm. raised greenish-brown papillary protrusion. Miscroscopic examination of the mitral valve revealed the cusp to be diffusely thickened due to fibrosis. The fibrous tissue was dense and hyalinized. At one point, the cusp was ulcerated and covered with a bulky mass of deeply eosinophilic fibrin material. Diagnosis: subacute vegetative endocarditis superimposed on an old rheumatic valvulitis.

The kidneys grossly demonstrated innumerable small dark-red punctate areas over the external surface. These were also scattered throughout the renal parenchyma. The external surfaces were smooth, with grey-white capsules which stripped easily. The right kidney weighed 220 Gm., the left 200 Gm. The calyces, pelves, ureters, and bladder were entirely normal. Microscopic section revealed involvement of all glomeruli (fig. 2). Some showed simple swelling of the epithelial cells, obliterating the lumen of glomerular capillaries rendering them ischemic. Other glomeruli demonstrated typical crescent formations. A large number of glomeruli contained fibrinous thrombi. Numerous tubules were distended with red blood cells. Diagnosis: subacute diffuse glomerulonephritis.

The cecum grossly presented many small punctate hemorrhagic areas in the submucosa. The external surface, however, appeared normal. Diagnosis: petechiasis of cecum.

Comment

It certainly would appear reasonable to assume that, in following a case of subacute bacterial endocarditis with complicating renal insufficiency, the exact pathological process in the kidney could be foreseen by the severity of the renal insufficiency. When true uremia becomes manifest clinically, the presence of a diffuse glomerulonephritis should be suspected. This is in contradistinction to the renal insufficiency, usually less severe, seen in focal embolic glomerulonephritis. Combinations of both types of glomerular disease may occur. Friedberg[3] states that four types of renal lesions may occur in subacute bacterial endocarditis: (1) focal embolic glomerulonephritis; (2) diffuse glomerulonephritis (which our case demonstrates); (3) renal infarction; and (4) combinations of the first three.

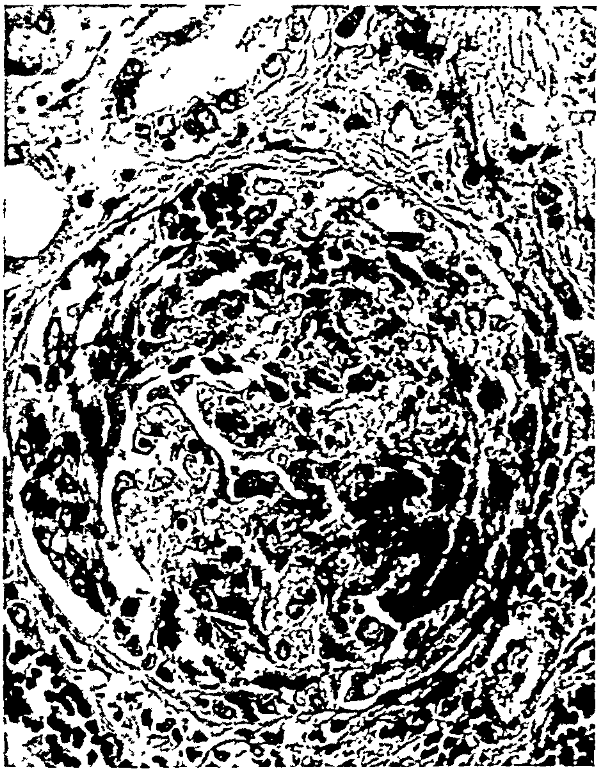

Fig. 2.—Microscopic section of kidney demonstrating diffuse glomerulonephritis.

No indisputable evidence has been presented to date to explain why one person with subacute bacterial endocarditis may develop any of the above renal lesions singly or in combination. Several years ago, Lillehei and co-workers,[4] in a series of experiments on dogs in whom large arteriovenous fistulas were constructed, were able to induce bacterial endocarditis in 100% of the animals by the intravenous introduction of small numbers of bacteria, although no cases occurred in animals without fistulas. Furthermore, 40% of the infected dogs developed acute proliferative glomerulonephritis in a week to five months after endocarditis occurred. These workers postulated that endothelial susceptibility was created in the heart and the kidneys by "cardiovascular stress." Certainly further work as to the more precise nature of this interesting corelationship remains to be done.

Summary

The occurrence of diffuse glomerulonephritis as a complication of subacute bacterial endocarditis is relatively infrequent. Focal embolic glomerulonephritis, diffuse glomerulonephritis, renal infarction, or combinations of these three types of lesions may occur as complications of subacute bacterial endocarditis. The precise nature of the corelationship of diffuse glomerulonephritis and subacute bacterial endocarditis remains to be established.

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DIAGNOSTIC VIROLOGY.—The rapidly expanding field of cellular virology has applied as well as fundamental scientific value. Practical applications of cell culture are helpful to the physician and to the epidemiologist (and indirectly, to the average citizen) for isolation of viruses and accurate assessment of individual or group immunity. The specific diagnosis of poliomyelitis, for example, and of many other virus infections is accomplished readily by cell-cultural methods. Virus is isolated and recognized by its ability to affect and destroy susceptible cells in culture, while the capacity of homotypic antibody to neutralize cytopathogenic potential of the virus permits identification of isolates. Cell cultures bring diagnostic virology within reach of all laboratories and offer reliable results obtainable almost as quickly as those required for diagnosis of other microbial infections.—J. T. Syverton, M.D., The Response of Mammalian Cells in Culture to Virus Infection, *Decennial Review Conference on Tissue Culture,* Oct. 8-12, 1956.

J.A.M.A., June 7, 1958

CLINICAL EXPERIENCES WITH WARFARIN (COUMADIN) SODIUM AS AN ANTICOAGULANT

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Coumadin sodium and bishydroxycoumarin were used in a study of the effects of anticoagulant therapy on 200 patients, most of them with acute myocardial infarction or severe coronary insufficiency. Coumadin sodium was given orally to 164 of these patients, the prothrombin times being determined daily. Individual dosages were adjusted until the daily dose (usually 5 to 7.5 mg.) needed to maintain the prothrombin level between 15% and 30% was found. Bishydroxycoumarin was given to 19 patients and dosages were similarly adjusted until the maintenance dose (between 20 and 100 mg. daily) was found. An additional group of 17 patients who at first received bishydroxycoumarin were shifted to therapy with coumadin sodium. Coumadin sodium was found to be far superior to bishydroxycoumarin. Coumadin sodium had the advantage of greater promptness of effect; it produced the desired prothrombin levels within 48 hours in 87% of the cases. Patients receiving it in maintenance doses were more likely to stay within the desired range of prothrombin levels. The frequency of side-effects (mainly hemorrhagic) was slightly though not significantly lower in the patients treated with coumadin sodium. Nine patients who exhibited bleeding phenomena promptly responded to withdrawal of the coumadin sodium or treatment with preparations of vitamin K.

A voluminous and, at times, controversial literature has accumulated during the past 15 years concerning the use of anticoagulant therapy in clinical medicine. Widespread interest in the use of anticoagulants for the treatment of acute myocardial infarction resulted from the early studies on bishydroxycoumarin (Dicumarol) both in the United States and abroad. A detailed study was begun in the United States by Dr. Irving Wright and the cooperative study group of the American Heart Association.[1] The varied opinions expressed[2] on the value of anticoagulants indicate that their routine use in acute myocardial infarction is by no means settled.

We have felt for some time that much of this uncertainty stemmed from difficulties encountered in using bishydroxycoumarin. The necessity for rigid laboratory control and daily or almost daily prothrombin time determinations, the unpredictability or the extent of the hypoprothrombinemic response resulting from a fixed initial dose of bishydroxycoumarin, the uncertain degree of intestinal absorption of the drug, the rather appreciable expense resulting from daily prothrombin determinations—all these factors helped generate differences of opinion concerning many aspects of anticoagulant therapy. We have been continuously interested, therefore, in attempts to find a more satisfactory anticoagulant for oral administration.

Recently a number of anticoagulant drugs have been introduced that offered some promise of being superior to bishydroxycoumarin. One that seemed to more nearly approach the ideal orally given anticoagulant than any of those previously described was warfarin (Coumadin) sodium. This is a report of observations in 200 patients treated at the Albert Einstein Medical Center, Philadelphia, with warfarin sodium or bishydroxycoumarin. Of the patients forming the basis of this study, 171 had acute myocardial infarction or severe coronary insufficiency, 6 had congestive heart failure, and 23 had phlebitis or some other thromboembolic disturbance.

Method

Of the 200 patients in this study, 164 were placed on orally administered warfarin sodium therapy. An initial dose of 1 mg. per kilogram of body weight was given, but we soon found it was not always practical to weigh patients. We then administered an initial dose of 60 to 75 mg., depending on the estimated size of the patient. A prothrombin time determination (by the Quick method) was obtained prior to the first administration of warfarin. Prothrombin times were then determined daily. Successive doses of warfarin sodium were varied with the daily prothrombin time, with use of the following schedule as a guide: (1) below 10%, no warfarin; (2) 10-19%, 2.5-5 mg.; (3) 20-29%, 5-10 mg.; (4) 30-39%, 10-15 mg.; and (5) above 40%, 20 mg. or more.

Experience soon led us to judge in each case the daily dose (usually 5-7.5 mg.) necessary to maintain the prothrombin level between 15% and 30%. Wherever possible, the warfarin was administered in the early afternoon after the day's prothrombin times were obtained. All prothrombin times were determined in the hospital laboratory. A total of 164 patients were treated with warfarin for 4 to 46 days. During this same time, 19 patients receiving

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bishydroxycoumarin were followed and, in addition, 17 patients begun on bishydroxycoumarin therapy were transferred to warfarin sodium therapy. Patients treated with bishydroxycoumarin were begun on 200 to 300 mg. and then given maintenance doses varying between 20 and 100 mg. daily.

Results

Our observations related primarily to four major aspects of anticoagulant therapy. One was the frequency and rapidity with which therapeutic hypoprothrombinemia was obtained after the initial dose of warfarin sodium. The second aspect of the study *concerned the length of time necessary to reach* therapeutic levels, which we considered to be between 15% and 30% of normal. The determination of the number of days that the prothrombin time remained within therapeutic levels and the dose necessary to maintain this level was a third essential consideration. Finally, we were concerned with the possibility of untoward reactions and the extension of pharmacological activity.

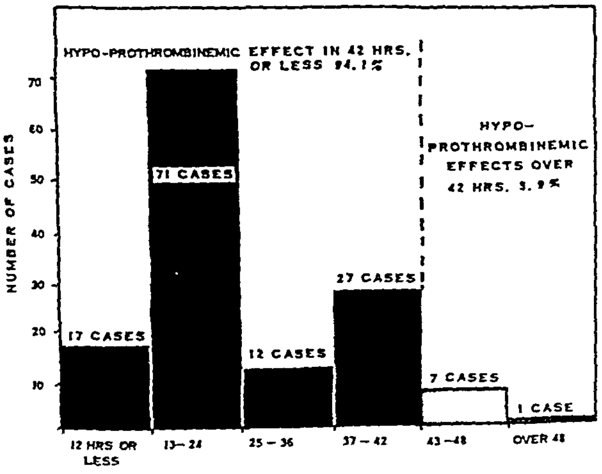

Fig. 1.–Beginning hypoprothrombinemic effect obtained with warfarin sodium therapy (135 patients).

These various aspects of warfarin therapy were evaluated in 181 patients, 17 of whom received both warfarin and bishydroxycoumarin. In 135 of the 164 patients receiving warfarin alone, we were able to determine the approximate time in hours from the administration of the drug to beginning therapeutic effects (fig. 1). In 88 patients (65%), hypoprothrombinemic effects were obtained in 24 hours or less and 94% exhibited therapeutic effects in 42 hours or less. This aspect of warfarin sodium therapy was actually evaluated in retrospect. Shapiro[3] has shown that many of his patients revealed beginning depression of prothrombin times within 8 to 12 hours of an initial oral dose of warfarin. In 141 of our cases we were able to determine the time necessary to reach the established therapeutic level, 15%-30% (fig. 2 and 3). In 123 cases (87%), true therapeutic levels were obtained in 48 hours or less. This is in sharp contrast to levels achieved with bishydroxycoumarin, which frequently requires 60 to 96 hours. In only one case, that of a patient with myocardial infarction and narcotic addiction, were we unable to reach therapeutic levels despite massive doses of warfarin.

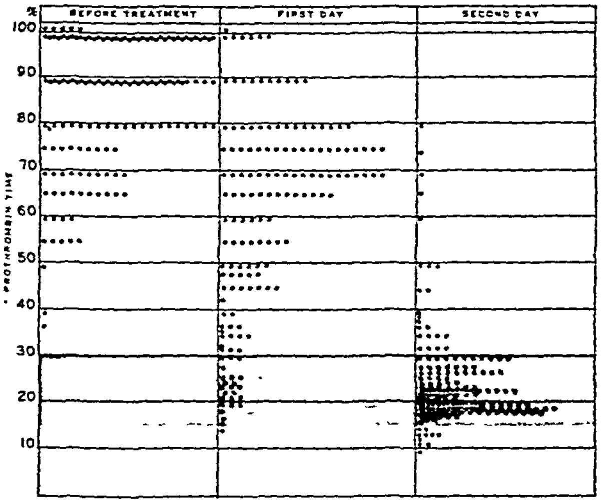

Fig. 2.–Depression of prothrombin time to therapeutic levels with warfarin sodium. (Each dot represents one patient.)

One of the disturbing aspects of bishydroxycoumarin therapy has been the frequency and unpredictability with which patients receiving this drug escape from therapeutic range. We found that only one-third of the 36 patients receiving bishydroxycoumarin were within therapeutic range 70-100% of the time; 22 patients (66.7%) were within therapeutic range less than 70% of the time (fig. 4). In contrast to this, we found that 132 (83.5%) of the 158 patients receiving warfarin for more than four days were within therapeutic range 70% or more of the time (fig. 5).

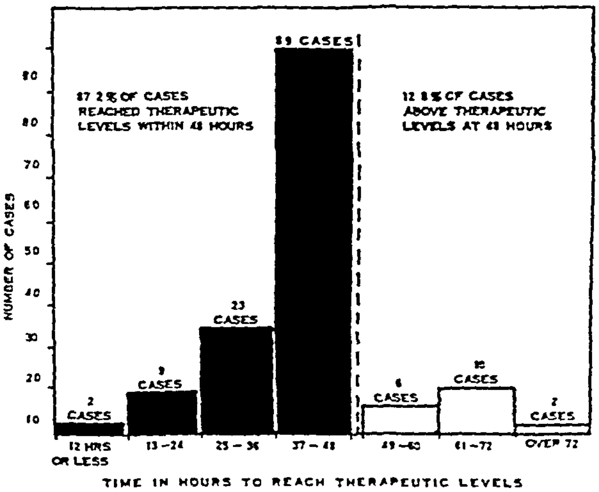

Fig. 3.–Time necessary to reach full therapeutic levels of prothrombin time with warfarin sodium (141 patients).

Toxicity and Untoward Reactions

Of the 19 patients receiving bishydroxycoumarin alone, 4 had untoward reactions. In two patients there was microscopic hematuria, in one rectal bleeding, and in one an unexplained fall in hemoglobin and hematocrit levels. The hematuria in both cases quickly disappeared as the dose of bishydroxycoumarin was decreased. In the patient with bleeding, a carcinoma of the colon was demonstrated. In the last case, there was no explanation for the fall in hemoglobin level, despite continued search for blood loss. Of the 181 patients receiving warfarin sodium, 9 exhibited bleeding phenomena as an extension of pharmacological effect. Three had gastrointestinal bleeding, two had bleeding gums or bloody sputum, one had hematuria, one had epistaxis, one had menorrhagia, and one had cutaneous petechiae. In the patients with gastrointestinal bleeding, we were able to demonstrate a benign antral ulcer, bleeding hemorrhoids, and carcinoma of the lung respectively. In eight of these nine cases with hemorrhagic complications, the prothrombin times were below 20% and bleeding promptly ceased when the warfarin was withdrawn or vitamin K or K_1 oxide was administered.

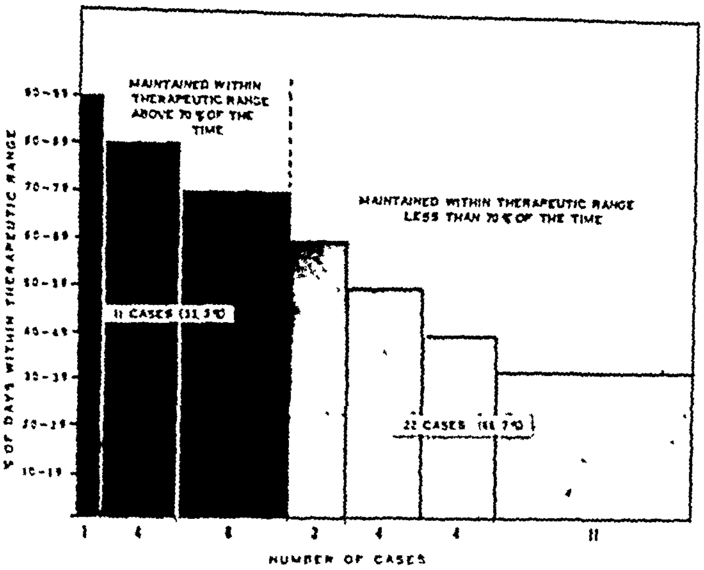

Fig. 4.—Days within therapeutic range with bishydroxycoumarin (33 patients).

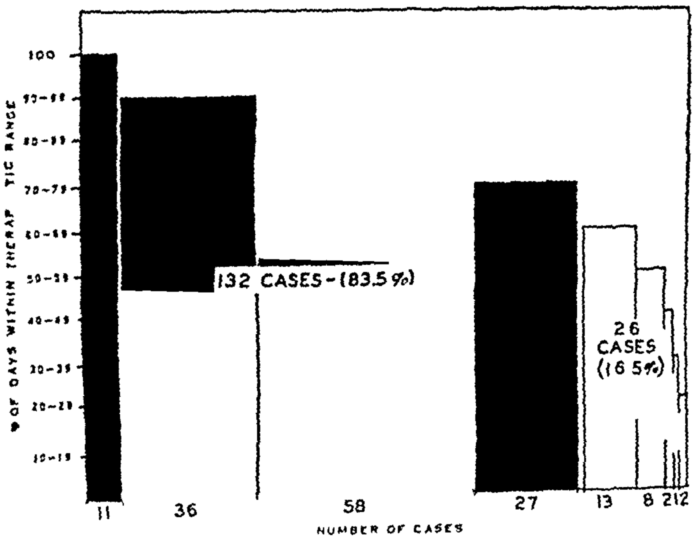

Fig. 5.—Days within therapeutic range with warfarin sodium (158 patients).

Comment

Extensive investigation firmly established the value of bishydroxycoumarin (Dicumarol) as the first effective orally given anticoagulant. However, objections and difficulties encountered in its use led to continued search for a more satisfactory anticoagulant. Ethyl biscoumacetate and cyclocumarol, two of the earlier coumarin derivatives, seemed superior in some ways to bishydroxycoumarin. Nonetheless, their use was attended by sufficient objections to prevent their widespread adoption as the "ideal anticoagulant."

The continued investigation of synthetic derivatives of bishydroxycoumarin by Link and his colleagues led to the development of warfarin sodium. (The recently introduced synthetic acenocoumarin investigated by Neill and others,[4] Manchester,[5] and Alexander and others[6] seems to have an almost identical chemical formula and quite similar hypoprothrombinemic effects.)

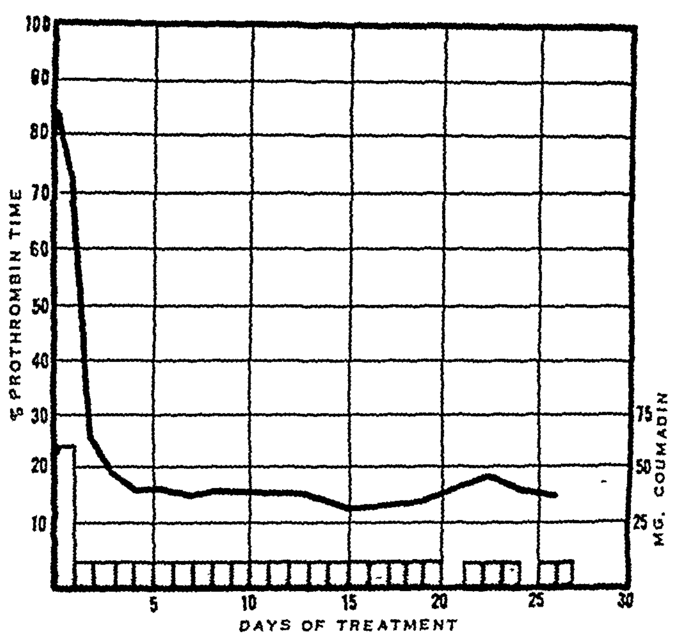

Fig. 6.—Levels of prothrombin time over 26 days in patient treated with warfarin sodium.

Our experience with warfarin has demonstrated its many advantages over bishydroxycoumarin. Pollock,[7] Clatanoff and others,[8] Shapiro,[3] and Goodman[9] have also suggested that warfarin more nearly approaches the ideal anticoagulant than any available drug to date. If the initial dose is adequate and given in one dose as recommended and if prothrombin levels are carefully followed in relation to the first administration of warfarin, therapeutic hypoprothrombinemia should be obtained in at least 95% of patients. Furthermore, the prothrombin level will be depressed to the therapeutic range of 15% to 30%, in 90% of the cases, in 42 hours or less. We found that the great majority of the 12.8% of our patients who required more than 48 hours to attain therapeutic levels had not received adequate amounts of warfarin the first or second day. Another distinct advantage of warfarin is the predictability of response and the ease with which the prothrombin level is maintained almost constantly and with very little fluctuation within therapeutic range. Figures 6 and 7 illustrate the smooth level of prothrombin times obtained in a patient with warfarin, in contrast to the variable levels obtained in another patient with bishydroxycoumarin. Prothrombin time tests done at the same time each day and the administration at a scheduled time of the day of the appropriate dose of warfarin, based on the results of the test, facilitate the ease with which the level is maintained within therapeutic range. Once the physician has gained experience in the use of warfarin sodium and the patient's pattern of prothrombin depression response to it is established, one can safely decrease the daily measurement of prothrombin times in the hospital to every second, third, or fourth day (fig. 8).

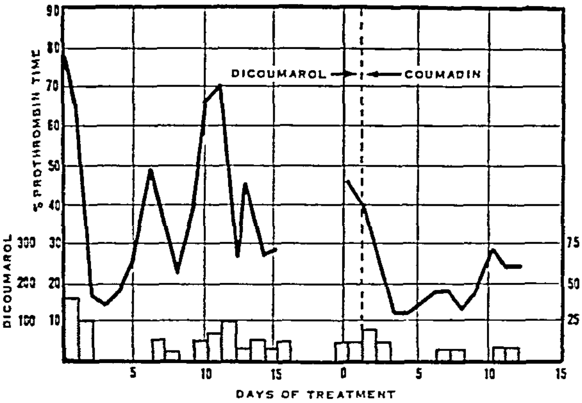

Fig. 7.—Levels of prothrombin time in patient treated with bishydroxycoumarin.

Our studies did not specifically include measurements of the time required for prothrombin levels to return to normal when warfarin sodium therapy was discontinued. However, Shapiro,[3] Pollock,[7] and other observers have demonstrated that hypoprothrombinemia after one dose of 75 to 100 mg. of warfarin will persist for two to five days. In those cases in which rapid elevation of the prothrombin level is desired, we have had no difficulty in mitigating warfarin effect by restoring the prothrombin time to at least 70% within 6 to 12 hours with whole blood, vitamin K, or vitamin K_1 oxide therapy.

One other aspect of anticoagulant therapy merits discussion. Little is yet known concerning the mechanism underlying the pathogenesis of atherosclerosis and vascular thrombosis. It is quite possible that disturbances in the clotting mechanism may play as important a part in the development of coronary thrombosis as disorders of fat and cholesterol metabolism. A number of studies in Norway and Russia during the last war suggested that when the caloric and fat intake were increased after relief of the blockade there was a fairly prompt increase in thromboembolic disturbances of all types. If there is any merit to these and related observations, there is then a logical basis for considering the value of long-term anticoagulant therapy. Warfarin sodium seems an ideal preparation for this purpose. Is this anticoagulant of any value in the long-term treatment of severe angina pectoris? Can it help retard the atherosclerotic process? Can it prevent recurrent coronary thrombosis and myocardial infarction? These questions are intriguing ones. Some studies with these thoughts in mind have already been published by Manchester and Putnam,[5] with use of acenocoumarin, and by a number of observers, with use of bishydroxycoumarin or one of its analogues. In our preliminary evaluation of long-continued warfarin therapy, we have easily maintained therapeutic hypoprothrombinemia in a number of outpatients, determining the prothrombin time at intervals of 10 to 20 days and using maintenance doses of 5 to 10 mg. of warfarin daily. We are now engaged in the further evaluation of long-term anticoagulant therapy in the prevention of coronary thrombosis and other thromboembolic disturbances in a larger series of ambulatory patients.

Summary

Hypoprothrombinemic properties of warfarin (Coumadin) sodium and bishydroxycoumarin (Dicumarol) were evaluated in 200 patients. Beginning therapeutic effect was accurately determined in 135 patients receiving warfarin; 65% exhibited therapeutic effects in 24 hours or less, and in 42 hours 94% exhibited beginning therapeutic effects. The time necessary to reach true therapeutic levels with warfarin was measured in 141 patients. In 123 (87%) true therapeutic levels of 15% to 30% were reached in 48 hours.

Of all patients receiving warfarin, 132 (83.5%) were within therapeutic range 70% of the time or more. This is in sharp contrast to results with bishydroxycoumarin; only 33.3% of these patients were within therapeutic range at least 70% of the period of observation.

The drug was easy to use, and prothrombin times were readily and smoothly controlled with small daily maintenance doses. There were no important

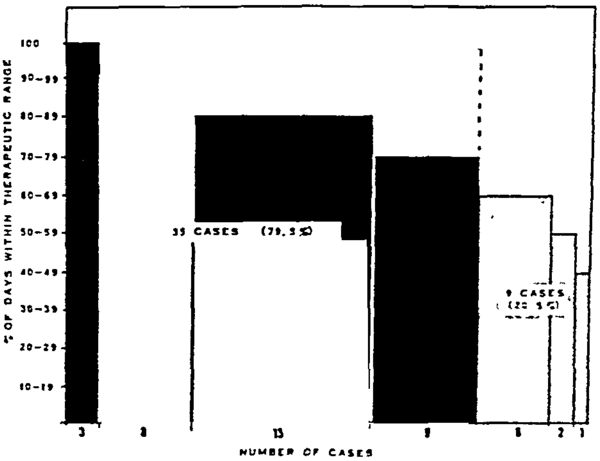

Fig. 8.—Days within therapeutic range with warfarin sodium, with intermittent prothrombin time determinations (44 patients).

side-effects, and the nine patients who exhibited bleeding phenomena promptly responded to administration of whole blood and vitamin K or K₁ oxide. Experiences in this study give further confirmatory evidence that warfarin is far superior as an anticoagulant to bishydroxycoumarin and that it most closely approaches the "ideal anticoagulant."

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The warfarin sodium used in this study was provided by Dr. Edward Barrett, medical director, Endo Laboratories, Inc., Richmond Hill, N. Y., as Coumadin sodium in 5, 10, and 25 mg. tablets.

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TREATMENT OF ALLERGIC RESPONSE TO PENICILLIN

PRELIMINARY REPORT

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Manifestations of allergy to penicillin, ranging from a mild rash with itching to giant urticaria and polyarthritis, were seen in 10 patients. In four of these the penicillin had been given prophylactically in connection with surgery. Medication consisting of 300 mg. of potassium salicylate, 300 mg. of sodium p-aminobenzoate, and 50 mg. of ascorbic acid, in the form of tablets given four times a day, completely relieved the allergic symptoms within 24 to 48 hours in nine of the patients. The 10th patient, who had had severe general reactions to a preparation of penicillin in the past, was enabled to take the same preparation without allergic reaction by taking the above medication prophylactically at the same time. Its use is still empirical, since it is not yet known which of the ingredients are active and how they interact, and further investigation is recommended.

Since the advent of the use of penicillin in medical practice, the development of an allergic response to this drug has not been uncommon. These reactions have varied from a mild erythematous eruption with severe itching to giant urticarial wheals and, in many cases, a polyarthritis of many months' duration. In the past, the treatment of this syndrome has been unsatisfactory. Antihistaminics are not as effective as might be wished; the steroids have been employed in some cases, but the use of these entails the risks which are inherent in any steroid therapy.

In an attempt to treat the polyarthritis associated with a penicillin reaction, a patient was given Pabalate (a composition of 300 mg. each of sodium salicylate and sodium p-aminobenzoate, with 50 mg. of ascorbic acid), one tablet four times a day. Within 48 hours, the arthritis, wheals, and hives which were present had completely disappeared. After a short period of time, the Pabalate therapy was discontinued and there was no reappearance of symptoms. This chain of events, except for the relief of the polyarthritis, was unexpected, and therefore the therapy was tried in several other patients to determine whether there was a causal relationship. The response obtained was the same.

Mechanisms Involved in Relieving Allergic Response

It is of interest to consider briefly the mechanisms which may be involved in relief of the manifestation of penicillin sensitivity. It has been shown[1] that the administration of salicylate causes an elevation of the ACTH level in the blood, and in some animals a depletion of adrenal ascorbic acid is noted after the administration of about one-half the lethal dose of salicylates. It has been further reported by other authors[2] that the physiological response to salicylates is similar to the response to ACTH or cortisone. However, it has not been shown that the administration of salicylates causes any increased urinary excretion of adrenocortical steroids,[3] and indeed other workers[4] have stated that the antirheumatic effects of salicylates appear to be neither related to nor dependent upon elevated circulating levels of adrenal steroids. It has been suggested that they may be due to an enhanced ability of the tissues to utilize the steroids, although it is possible that salicylate action is in no way related to adrenal hormones. Some investigators have believed that such agents as aspirin may both exhibit a stimulating effect on the pituitary gland and effect an increase in the rate of removal of the steroids from the circulation by means other than urinary excretion.[5]

Zarafonetis[6] has published papers on the use of potassium *p*-aminobenzoate in the treatment of a variety of collagen diseases and in dermatitis herpetiformis. One patient with dermatitis herpetiformis reported in 1952 was treated with potassium *p*-aminobenzoate which caused an initial flare, followed by improvement of the pruritus, although the eruption remained virtually the same.[7] In 1952, 20 patients with various inflammatory skin diseases were given sodium *p*-aminobenzoate by mouth in daily doses ranging up to 16 Gm. for periods of two weeks to several months. Results were variable, but the authors[8] felt that they had achieved cures in some cases at least of atopic dermatitis and contact dermatitis and a transient response in a patient with dermatitis herpetiformis. In 1950, Ricci[8a] reported that orally given *p*-aminobenzoate caused an immediate therapeutic response in 34 infants and children suffering from serum sickness after the administration of diphtheria antitoxin. Five untreated patients used as controls experienced a more severe and prolonged illness.

Other authors have pointed out a synergistic action between *p*-aminobenzoic acid and salicylates, and it has been demonstrated that the concurrent administration of both agents increases the salicylate concentration in the blood above that which is achieved when the salicylate in the same dosage is administered alone.[9] Good and his associates[10] have demonstrated the ability of combined *p*-aminobenzoic acid and salicylate therapy to reduce from 90% to 10% the incidence of experimentally produced allergic acute disseminated encephalomyelitis in guinea pigs. Neither *p*-aminobenzoic acid nor salicylates alone gave this order of protection even when salicylate intoxication was induced.

The functions of vitamin C in the body are many and varied. Recently Reppert and co-workers[11] have drawn attention to the speed with which ascorbic acid corrects the capillary fragility in scurvy, and their work indicates that ascorbic acid in large doses inhibits the hyaluronidase–hyaluronic acid reaction and that this inhibition of the "spreading factor" may account for the rapid improvement noted. It has also been noted by Long and his associates[12] that orally given ascorbic acid desensitized BCG-infected guinea pigs to intradermally injected tuberculin. The role of vitamin C in adrenal function is still the subject of much investigation and question. However, it is apparent that an intimate relationship exists between vitamin C and the corticosteroids.[13]

From the preceding brief discussion, it can be readily seen that the activity of Pabalate in penicillin sensitivity may be theoretically ascribable to any one of the individual components. Due to the present widespread use of salicylates and ascorbic acid as contained in multiple vitamin preparations, it is more likely that the *p*-aminobenzoic acid plays a major role either alone or in synergism with one or more of the other components. This has yet to be established and will be the subject of future work.

Report of Cases

Case 1.—A 27-year-old male with no previous history of allergies underwent a rib resection for an osteochondroma, and the patient was placed on penicillin therapy postoperatively as a prophylactic measure. One week after penicillin therapy, he developed a polyarthritis that was characterized by remissions and exacerbations and that affected different joints at different times. He also developed hives, with moderate to severe itching. He was treated for a period of several weeks with antihistaminics, which had no effect. Pabalate, one tablet four times a day, was administered as therapy for the polyarthritis. Forty-eight hours later the patient returned to report that no further outbreaks of his arthritis had occurred and that, in addition, his wheals and hives had no longer been in evidence. From this point on, he was completely free of any symptoms of an allergic nature. In this instance it was felt that the Pabalate probably helped his arthritis, but no explanation could be given for the disappearance of the urticaria and hives.

Case 2.—A 47-year-old female was seen at her home with a generalized erythematous eruption and severe itching. Forty-eight hours previously she had received penicillin. She had a generalized edema of the face, and her periocular tissues were edematous, causing her palpebral slits to be markedly narrowed. A diagnosis of penicillin sensitivity was made. The patient was given Pabalate, one tablet four times a day. In 24 hours her itching had been relieved, and the rash had faded to about one-half of its former extent. Within 48 hours she was completely back to normal, with no further itching and no further rash. Therapy was discontinued in this case.

CASE 3.—A 32-year-old man had been treated six months prior to examination with a course of penicillin. He developed a polyarthritis which was characterized by remissions and exacerbations, affecting different joints on each exacerbation. He had been treated at different times by the physician who had originally used the penicillin but had gained no relief from any of the drugs employed. He had learned from other patients that I had a "miracle cure" for this condition and hence called upon me. He was given Pabalate, one tablet four times a day. Forty-eight hours later he phoned to report that he had no further polyarthritis and was completely asymptomatic.

CASE 4.—A 4-year-old boy received a severe laceration of the tongue, which was sutured with the patient under general anesthesia in the operating room. He was given penicillin orally as a prophylactic measure. Twenty-four hours postoperatively the mother phoned to report that the child had measles or poison ivy, as he had broken out with a severe erythematous rash and complained of severe itching. The mother was reassured that this was penicillin reaction and was advised to discontinue administration of penicillin. Four ounces of Pabalate liquid was prescribed, with directions to take one teaspoonful four times a day. The mother called 24 hours later to report that the rash had disappeared and that there was no further itching. Pabalate therapy was discontinued. The lad was seen in the office one week later, and he showed no further evidence of any reaction to the penicillin.

CASE 5.—A 52-year-old woman was given penicillin prophylactically after a panhysterectomy. Her daughter, a trained nurse, telephoned on the patient's seventh postoperative day to state that her mother had urticarial wheals on her upper arms and chest. Pabalate, one tablet four times a day, was prescribed. Twenty-four hours after medication was instituted, the wheals disappeared and did not recur.

CASE 6.—A 37-year-old female was treated for acute follicular tonsillitis. She was given Biosulfa 250 (a composition containing 250,000 units of crystalline potassium penicillin G, and 0.167 Gm. each of sulfadiazine, sulfamerazine, and sulfamethazine), and 48 hours after the institution of penicillin therapy she called to report an erythematous eruption with itching. The penicillin medication was discontinued and Pabalate, one tablet four times a day, was prescribed. Twenty-four hours after institution of Pabalate therapy the patient reported that the rash had disappeared and that she had no further itching or signs of an allergic reaction.

CASE 7.—A 26-year-old female underwent a panhysterectomy, and penicillin injections were ordered prophylactically. Forty-eight hours postoperatively the patient developed an erythematous eruption and complained of itching. Penicillin therapy was discontinued. Pabalate, two tablets every four hours, was prescribed. After five doses of this medicament, the rash disappeared, the pruritus disappeared, and the patient had no further difficulty.

CASE 8.—A 73-year-old woman had been given penicillin one week previously by another physician and developed a severe rash with itching. She was treated with antihistaminics to no avail. Pabalate, one tablet four times a day, was prescribed, and the patient reported complete relief in 48 hours.

CASE 9.—A 29-year-old male was seen with acute follicular tonsillitis. He was advised that penicillin therapy would be the best regimen of treatment for this situation. He became quite alarmed because on two previous occasions he had been given penicillin and had broken out with hives accompanied by severe itching. He had been warned by his doctor to caution any physician in the future against administering penicillin to him. For the first time, the opportunity presented itself to institute Pabalate therapy prophylactically. The aforementioned cases were cited to him briefly and it was brought out that I desired to use Pabalate prophylactically to prevent an allergic response to penicillin. His cooperation was sought and he agreed to try it. Penicillin was given orally in the form of Biosulfa 250 and also Pabalate, one tablet four times a day, to be taken concurrently with the other medicament. During the course of treatment, no evidence of allergy developed nor did any allergy develop after medication was discontinued.

CASE 10.—A 21-year-old female was seen with acute follicular tonsillitis. Eighteen months previously she had been treated with penicillin and had developed a severe, generalized erythema and urticaria. At that time she had been treated also with Pabalate, with remission of her symptoms in 24 hours. It was requested that she take penicillin and the drug that had relieved her of her symptoms previously. She was reassured that in all probability an allergic reaction would not develop when both drugs were taken simultaneously. She agreed to try it and was given Biosulfa 250, the product to which she had been allergic previously, and Pabalate, one tablet four times a day, to take at the same time. During her course of therapy, no reaction occurred to the penicillin, and there were no allergic responses after treatment was discontinued.

Summary

Pabalate (a composition of 300 mg. each of sodium salicylate and sodium p-aminobenzoate, with 50 mg. of ascorbic acid) has been used in the treatment of penicillin sensitivity reactions. It is impossible to say at this time whether a single component is the active material or whether there is a synergistic action between two or more of the compounds included in the formulation. The use of Pabalate in the treatment of penicillin sensitivity reactions warrants further investigation.

988 Mammath Rd.

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CORONARY HEART DISEASE IN FORMER FOOTBALL PLAYERS

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The health records of a group of 355 men who had distinguished themselves at football in the years 1901 to 1930 inclusive were studied for factors that might predispose a man to coronary heart disease. The cause of death was ascertained in 87 cases and was found to be coronary heart disease in 25. Comparisons were made between former athletes still living without coronary heart disease and former athletes, living or dead, with coronary heart disease, with respect to data that had been recorded during health examinations while they were in college and noted in the years since their graduation. The coronary and noncoronary groups did not differ significantly with respect to body build as recorded in college, but the family histories of the coronary group showed a higher incidence of unfavorable family health and the coronary group gained more weight after leaving college. Little difference was found in this study between heavy smokers and abstainers and between heavy drinkers and abstainers, but it is noted that the groups were small and did not manifest any wide diversity in ways of life. The most interesting finding concerned the amount of exercise taken habitually during the lifetime of these men. Those in the coronary group engaged in less vigorous exercise than did the others, and no individual in this study who maintained a heavy exercise program happened to develop coronary heart disease.

The health and longevity of athletes has been of considerable interest for 100 years or more and is still a problem of great importance. Not many satisfactory studies have been carried out and published concerning this question, especially as it relates to so-called heart strain and the development of heart disease. Now and then, in the past, some interesting observations have been made, which include a book entitled "University Oars," by Morgan, dated 1873, which discusses the longevity of members of the Oxford and Cambridge crews in the years 1829-1869. Dr. Morgan concluded as follows:

> On the whole the results obtained by the Life Tables, in so far as they bear upon the duration of life of the Cambridge University Oarsmen, must be deemed decidely favourable; the lives of each one of the 32 crews to which they refer extended over 334 instead of 320 years (expected for the male population at large). Hence each individual who rowed is likely to survive the race, on an average, some 42 instead of 40 years.
>
> The lives of the Oxford men are on the whole decidedly better than those of the Cambridge Oars, the former averaging 43.7 years instead of 40 after the race. This is due to the fact that out of the 16 Oxford crews which rowed between 1829 and 1869 only 15 men died within those years, while the deaths among the Cambridge men, who took part in the same races, amount to 24.

Dr. Morgan stated that 11 men died from fever, 7 from consumption, 2 from other forms of chest disease, 6 from accidental causes, 3 from heart affections, 2 from diseases of the brain, 2 from inflammatory attacks, 1 from general paralysis, 1 from calculus, 1 from erysipelas, 1 from Bright's disease, 1 from cancer, and 1 from lupus erythematosus.

Another report of interest was that of Gaines and Hunter, who wrote a paper entitled "Mortality Among Athletes and Other Graduates of Yale University" in the *Transactions of the Actuarial Society of America*, in 1905. The author summarized some of the results as follows:

> Combining crew, football, track and baseball and tracing members to the end of 1904, the death rate was nearly 25 *per cent lower than* among graduates of the Academic Department. Among the 55 deaths there were 12 from tuberculosis of the lungs and 5 from typhoid fever, conditions which would not appear nowadays. A synopsis of the experience of the Yale graduates from 1701 through 1777 indicates a high death rate at ages under 35, nearly three times that in this present generation. It was not until the age group 70 *and over that the mortality* rates compare with the current ones.

It is well known that coronary heart disease tends to be more common in men of the mesomorphic body type than in those of other (endomorphic and ectomorphic) types. In view of this propensity, it was believed to be desirable to study a group of individuals with this body build, with reference to the possible influence of various environmental factors upon the coronary circulation.

Present Study

It was hoped that Harvard football lettermen of a generation ago would furnish a suitable group for a study of this sort. Questionnaires were sent to all "H" winners in football for Harvard from 1900 to 1930 (except the years 1918 and 1919 when no intercollegiate games of football were played by Harvard because of World War I). Further information was obtained where possible by individual letters to families and to personal physicians. Also, the death certificates for the Commonwealth of Massachusetts were examined for causes of death in cases where no other information was available.

TABLE 1.—*Causes of Death of Eighty-seven Harvard Football Players of a Generation ago*

Causes of Death	Cases No.	Cases %
Coronary heart disease (thrombosis or angina pectoris)*	25	28.8
Malignancies and tumors	11	12.6
Pneumonia	9	10.3
War injuries	9	10.3
Accidents	8	9.2
Suicide	4	4.6
Cerebral hemorrhage*	3	3.4
Typhoid	2	2.3
Generalized arteriosclerosis*	3	3.4
Nephritis	2	2.3
Uremia	2	2.3
Congestive heart failure*	2	2.3
Miscellaneous (1 case each)	7	8.0

* Cardiovascular disease in 33 (37.9%) apparently was due to arteriosclerosis or/and hypertension without congenital, rheumatic, or syphilitic heart disease.

According to the Harvard College alumni records, 424 men won football "H's" in the years 1901 to 1930 inclusive. Of these, 292 were known to be alive, 6 were lost to follow-up, and 126 were known to have been dead as of the date of 1955 on completion of these data. The cause of death was known for 87 of the 126 men. Of the grand total of 424, some information was available concerning 355 persons. It is of interest that, of these, 34 were known to have or to have had definite coronary heart disease.

TABLE 2.—*Causes of Death of Adult White Males in Massachusetts in 1940*

Causes of Death	Deaths No.	Deaths %
Diseases of circulatory system	10,081	42.0
Chronic myocarditis and myocardial degeneration*	3,988	16.6
Other diseases of myocardium	697	2.9
Diseases of coronary artery	3,477	14.5
Angina pectoris	127	0.5
Chronic affections of valves and endocardium	688	2.9
Other diseases of circulatory system (including 351 cases of arteriosclerosis)	1,107	4.6
Suicide	424	1.8
Cancer and other tumors	3,273	13.6
Accidents	1,359	5.7
Cerebral hemorrhage	1,690	7.0
Pneumonia	1,165	4.8
Typhoid	6	0.0
Chronic nephritis (not arteriosclerotic kidney)	863	3.6
Acute nephritis	24	0.1
All other causes†	5,138	21.3
Total	24,026	100.0

* Includes hypertensive heart disease.

† Includes tuberculosis, 1,015 cases; diabetes, 535; cirrhosis of liver, 265; diseases of digestive system, 866; arteriosclerotic kidney, 526; and hypertrophy of the prostate, 266.

Findings

The causes of death in 87 former football players are enumerated in table 1. For purposes of comparison, the causes of death in adult white males in Massachusetts for the year 1940 are listed in table 2. These data were chosen because the median year of death for the group being studied was 1936, and the vital statistics for 1940 were the nearest available for Massachusetts.

A comparison of the percentages of coronary disease in the two groups is difficult because of the vague nature of "chronic myocarditis and myocardial degeneration." Certainly many of these are cases of hypertensive or coronary heart disease. If the cases attributed to cardiovascular disease in each group are compared, it is noted that the former football players have but a slightly lower percentage of death from that cause. It is presumed, of course, that the football players were free of rheumatic and congenital heart lesions at the time of their participation in the sport. They were all carefully examined at that time.

An attempt was made to compare the longevity and mortality of these Harvard football players with that of healthy males of comparable age in the general population or indeed among Harvard graduates who had not played football, but adequate data for any such statistical comparison were lacking. The principal objective of the study, the evaluation of the influence of various factors upon the incidence of coronary heart disease in this group, was approached in two ways.

Table 3.—*Comparison of Data of Exfootball Players With and Without Coronary Heart Disease*

General Data	Group Living Without Coronary Disease, per Class Grouping 1901-1905	1906-1910	1911-1915	1916-1920	1921-1925	1926-1930	Coronary Group, Both Dead and Living
Body build							
Av. height in college, ft.-in.	6-0	5-11½	5-11	6-0	5-11½	5-11½	5-11
Av. weight in college, lb.	173	184	171	187	182	179	182
Av. weight in later life, lb.	175	190	182	199	193	190	200
Marital status, %							
Married	95	86	88	100	98	91	90
Unmarried	5	9	12	0	2	7	3
Divorced	0	5	0	0	0	2	7
Children, av. no.	2.6	2.0	2.4	2.2	2.6	2.3	2.5
Family history of coronary heart disease, %							
None	67	71	62	82	67	57	67
Mild	0	5	0	0	2	6	0
Moderate	33	14	38	18	26	31	13
Severe	0	10	0	0	5	6	20
Habits of exercise, %							
None	0	5	4	8	0	1	18
Minimal	5	32	15	15	17	31	12
Light	19	32	22	31	38	23	52
Moderate	71	22	55	38	37	39	18
Heavy	5	9	4	8	8	6	0
Use of tobacco, %							
None	14	9	26	8	23	25	18
Unspecified amount	10	18	11	8	6	8	10
Minimal	14	14	0	0	3	3	0
Moderate	48	41	33	46	38	34	28
Heavy	14	18	30	38	29	30	44
Use of alcohol, %							
None	0	18	22	8	14	9	11
Unspecified amount	5	18	7	8	5	7	5
Minimal	29	23	4	8	8	11	21
Moderate	57	41	56	76	67	65	52
Heavy	9	0	11	0	6	8	11
Caloric intake, %							
Moderate	100	86	100	67	90	96	77
Heavy	0	14	0	33	10	4	23
Fat intake, %							
Light	20	14	17	0	24	8	0
Moderate	80	72	83	100	59	84	75
Heavy	0	14	0	0	17	8	25
Cholesterol intake, %							
Light	20	0	17	33	10	4	0
Moderate	80	57	50	67	59	64	83
Heavy	0	43	33	0	31	32	17

First, the lettermen with known coronary heart disease were compared with a control group in reference to the factors under study. As a control group, the former football players who are living and have no evidence of coronary heart disease were chosen. The comparison between the coronary group and the control group is made in table 3. It will be noted that the control group is broken down into groups of five graduating classes (1901 to 1905, 1906 to 1910, and so on). This breakdown was made so that it would be possible to note any changing trends during the 30 years covered by this study.

If table 3 is examined, it will be seen that the body build in college of the coronary group did not differ significantly from that of the control group. The coronary group did, on the whole, gain more weight than the control group. There was a definite difference here, though not of great magnitude. The family status of the coronary group does not differ markedly from that of the control group except that there were more divorces in the group with coronary heart disease. This may or may not represent a factor of stress. With reference to a family history of coronary heart disease, the ex-athletes who eventually developed coronary heart disease had a definitely higher occurrence of "unfavourable family health." This meant, in most cases, that both parents had had coronary heart disease.

Table 4.—*Comparison of Extremes in Data on Weight Gain, Exercise, and Use of Tobacco and Alcohol in Exfootball Players*

Current Data	Classes, No. of Persons 1901-1905	1906-1910	1911-1915	1916-1920	1921-1925	1926-1930	Total
Marked weight gain (40 lb. or more)							
Living and well	0	2	1	2	6	8	19
Coronary heart disease	2	2	2	0	0	1	7
Other significant disease	4	0	3	0	0	5	12
Little or no weight gain (5 lb. or less)							
Living and well	3	1	1	2	5	8	20
Coronary heart disease	1	3	0	0	0	0	4
Other significant disease	6	2	5	1	2	5	21
Heavy exercise							
Living and well	0	0	1	1	3	4	9
Coronary heart disease	0	0	0	0	0	0	0
Other significant disease	1	2	2	0	2	1	8
Little or no exercise							
Living and well	1	5	2	3	10	21	42
Coronary heart disease	2	1	1	0	0	2	6
Other significant disease	1	4	3	0	1	7	16
Heavy smoker							
Living and well	2	4	4	5	15	20	50
Coronary heart disease	0	1	3	0	2	0	6
Other significant disease	1	2	4	2	4	7	20
Nonsmoker							
Living and well	3	3	3	1	10	9	29
Coronary heart disease	0	1	2	0	0	1	4
Other significant disease	2	0	4	0	5	12	23
Heavy drinker							
Living and well	1	0	0	0	2	4	7
Coronary heart disease	0	1	0	0	1	0	2
Other significant disease	1	0	3	0	2	3	9
Nondrinker							
Living and well	0	3	2	1	5	5	16
Coronary heart disease	1	0	1	0	0	0	2
Other significant disease	0	2	4	0	2	3	11

The most interesting finding of the entire study concerned the amount of exercise. As can be seen from table 4, the men in the coronary heart disease group engaged in less vigorous exercise than did those without heart disease. The objection might be raised that these figures are from the period after the onset of heart disease and thus represent a curtailing of normal activity. This is not the case, since the lifelong habits of exercise were investigated. This is an important finding.

With reference to the use of tobacco, there were a few more heavy smokers than nonsmokers in the coronary heart disease group. This is not of statistical significance. The use of alcohol was about the same in both groups.

With reference to diet, it is difficult to draw definite conclusions because of the probable inaccuracies of estimation by those filling out the questionnaires. There seems to be little difference with reference to caloric intake. The coronary group generally ate more fat than did the control group, though, as noted above, all of the figures relating to diet are open to question.

The second method of investigating the effect of the various factors being studied was the comparison of the extremes in each instance. These data are listed in table 4 by number of cases. If the "H" men who gained 40 lb. or more are compared with those who had little or no weight gain, it can be seen that there was an increased risk of developing coronary heart disease in those with the marked weight gain. With reference to exercise, although there were relatively few exathletes who continued a strenuous program of physical activity, it appeared that a heavy exercise program tended to protect against coronary disease. On the other hand there seemed to be little difference between heavy smokers and abstainers and between heavy drinkers and abstainers with reference to the development of coronary heart disease, although there were but limited numbers in both of these groups; the average Harvard graduate used tobacco and alcohol in a moderate degree.

Summary and Conclusions

A questionnaire study has been made of the prevalence of coronary heart disease in mesomorphic exathletes and of the influence of various environmental factors upon its development. An attempt was made to follow up 424 Harvard College students who won their football H's in the years 1901-1930 inclusive. Of these, in 1955, 126 were known to have died and 292 to be alive; 6 could not be traced. The cause of death was known in 87 of the 126. Among these, coronary heart disease was responsible for 25 deaths, or 29%. Cerebral hemorrhage, generalized arteriosclerosis, and congestive heart failure accounted for 8 more cases, making the total 33 cardiovascular deaths, or 38%. Cancer apparently caused 11 deaths, or 13%; pneumonia and war injuries 9 deaths each, or 10%; accidents 8 deaths, or 9%; suicide 4 deaths, or 5%; typhoid 2 deaths; and the balance miscellaneous.

An attempt was made to compare these figures with those of the white male population of the same age-group in Massachusetts in whom cardiovascular deaths amounted to 44%, cancer 13%, accidents 7%; and pneumonia 5%. The cardiovascular deaths included an uncertain number of cases of coronary heart disease labeled as such in 13% and probably included under the designation of chronic myocarditis or degeneration, which was recorded as 16%. The mortality of these football players as compared with healthy males of the same age in the general population could not be determined because of the inadequacy of data.

The following relationships in the group of football players were compared for persons whose history showed the presence of coronary heart disease and for those without coronary heart disease: body build, weight gain, personal family status, family history, habits of exercise, use of alcohol and tobacco, and diet.

Body build did not differ significantly, but there was more weight gain in the coronary group than in the other. The family status was not significantly different except that there were more divorces in the coronary group. There was a higher percentage of family history of coronary heart disease in the coronary group than in the control group. One of the most significant findings in the study was the apparent protection afforded by the continuation of a program of heavy exercise. Those who maintained even moderate habits of exercise were less prone to coronary heart disease, and no individual in this study who maintained a heavy exercise program happened to develop coronary heart disease. There was a higher percentage of heavy smokers in the coronary group, but the difference was not marked. Alcohol appeared to have little influence on the development of coronary heart disease. The lack of detailed and accurate information about the dietary habits prevented any satisfactory conclusions in that area.

The chief defect revealed in a study of this sort lies in the uniformity of the ways of life of most Harvard and other college graduates and, therefore, in the difficulty of comparing extremes because of the inadequate numbers represented therein. A study of racial groups, of which certain members, either in the country of their origin or when transplanted elsewhere, live very differently from others of the same race, should prove more instructive.

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MULTIPLE CAUSES OF IRON DEFICIENCY IN INFANTS

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The possible causes of hypochromic anemia were sought in a study of 272 infants whose blood had been found to contain less than 9 Gm. of hemoglobin per 100 cc. The most common factor was prematurity or a birth weight of less than 3,000 Gm. Prematurity was present in 80% of the patients with a hemoglobin concentration of less than 5 Gm. per 100 cc. The incidence of severe hypochromic anemia in infants weighing more than 4,000 Gm. is extremely low. A first child was less liable to become anemic than were later siblings; single children were less liable than twins; and girls less liable than boys. Dietary information was incomplete, but the most frequent dietary pattern, before treatment, was found to have been two quarts of milk daily, supplemented with mashed potatoes, dried beans, crackers, or bread. The evidence showed, however, that deficient iron intake was not the sole cause of severe hypochromic anemias. Prevention therefore depends largely on the recognition of susceptible infants in the population. These should be watched carefully and treated prophylactically with adequate doses of medicinal iron.

Despite an increasing body of knowledge concerning iron metabolism, the incidence of hypochromic anemia approaches 30% of infants in the second year of life in at least one large pediatric clinic.[1] The continued occurrence of a preventable disease in such a large number of infants is a shocking public health problem. The prevention of iron deficiency and its associated hypochromic anemia depends on sound knowledge concerning its etiology.

Present knowledge of iron metabolism in infants[2] suggests four possible mechanisms for the development of iron deficiency. The first is deficient stores of iron at birth. The amount of iron in the circulating hemoglobin and in the tissues of the newborn infant can be reduced because of maternal deficiency or by blood loss during the perinatal period. A second possibility is the relative growth rate. Small infants, especially premature infants, tend to grow faster in relation to their birth weight. The demands of the body for iron are increased. The relatively rapid expansion of the hemoglobin mass is a major component of the iron needs. A third possibility is a deficient intake of iron by the infant. Iron deficiency anemia has been known as "nutritional anemia" and "milk anemia" because of the recognized importance of the iron intake in its development. Defects in absorption of iron should be considered as conditioned iron lack in this category. A fourth possible mechanism is blood loss; this is the most common mechanism of development of iron deficiency in adults. Chronic blood loss may be an important cause of iron deficiency in infants harboring hookworm and other parasites. Its frequency in their absence is unknown. An attempt to define the relative importance of these factors in the pathogenesis of hypochromic anemia in infancy is the subject of the present study.

Description of Sample

A survey of three years of experience with hypochromic anemia in this clinic has been made as a background for a broader program for investigation of iron metabolism in infants. All the infants in this study had a hemoglobin concentration of less than 9 Gm. per 100 cc. and either a mean corpuscular hemoglobin concentration (MCHC) of less than 30% or a definite response to iron therapy. These criteria indicate anemia of at least moderate severity and avoid confusion with physiological variations in hemoglobin concentration. The data analyzed in this report were obtained from the hospital records and were limited to those items considered to be equally valid for all of the cases studied. These patients were seen in either the outpatient department or the wards of Vanderbilt University Hospital between Jan. 1, 1954, and Dec. 31, 1956. Many of these infants were admitted for the treatment of acute illnesses. While this group of patients is more characteristic of the experience of an active pediatric service than of the population at large, it is felt to be a representative group of anemic infants.

Results

A total of 272 cases of hypochromic anemia was seen during this three-year period. The yearly frequency was related to the total number of visits to the outpatient department and hospital of children under 16 years of age (excluding newborn infants and well babies). In 1954, in a total of 9,833 visits, 69 cases (0.70%) were determined; in 1955, 78 (0.76%) in 10,223 visits; and in 1956, 125 (1.13%) in 11,057 visits. The more frequent oc-

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currence in 1956 represents my interest in collecting cases. This has resulted in the inclusion of many which were diagnosed and treated without being recorded by means of a formal diagnosis. There is every reason to suspect that a similar incidence occurred in the two previous years. No seasonal trend could be identified.

The age distribution of the cases is shown in table 1. Only one instance of hypochromic anemia was diagnosed in a patient more than 5 years old.

Table 1.—*Age Distribution of Patients with Anemia*

Age, Mo.	Cases, No.	
	Total	In Premature Infants
0- 6	6	4
7- 9	50	21
10-12	70	20
13-15	44	15
16-18	40	12
19-21	21	6
22-24	10	1
25-27	12	...
28-30	4	...
31-60	12	...
Total	272	79

His anemia was iatrogenic and developed during the study and treatment of a complex metabolic problem. This case has been omitted from the compilation. All but 12 cases occurred in patients under the age of 30 months. In the remainder, the ages were rather evenly distributed between 30 and 60 months. Anemia was recognized in the premature infants before the age of 24 months.

The data on race and sex are presented in table 2. The population of our outpatient department is approximately 40% Negro. The disease incidence of 36% in Negro infants does not suggest any racial differences. Anemia was more frequent in male infants than in females. With the exception of the full-term white infants this difference was statistically significant in the subgroups presented in table 2.

Table 2.—*Sex Ratio of Patients with Hypochromic Anemia*

			Male			
Birth	Race	No.	Found, %	Expected*, %	Chi-square	P
Term	White	119	53 8	51.9	0.162	Not significant
	Negro	50	71.3	51.5	8.19	0.004
Premature	White	44	63.6	46.2	4.74	0.03
	Negro	35	71.4	42.6	10.78	0.001
Total	White	174	58.0	51.5	2.99	Not significant
	Negro	98	71.5	50.4	16 49	0 001

* Duffield and others: Child 5:123, 1940.

The distribution of 254 patients with anemia by birth weight is compared in figure 1 with the birth weight distribution of total live births in Tennessee in 1954. Sex and race differences in birth weight have been omitted from the figure since they were small when compared to the deviation of this group of patients from the population as a whole. The total incidence of prematurity (including twins) was 31.1%, subdivided as follows: white males, 30.4%; Negro males, 38.5%; total males, 33.7%; white females, 22.5%; Negro females, 38.5%; total females, 26.8%; total white births, 27%; and total Negro births, 38.5%.

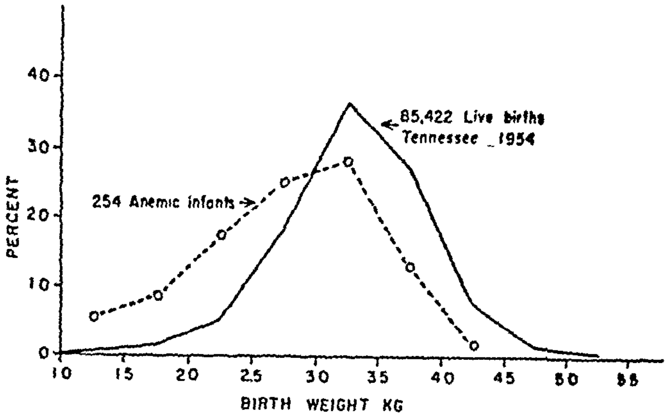

Fig. 1.—Birth weight distribution of 254 patients with hypochromic anemia of both sexes and both races compared with that of total live births in Tennessee in 1954.

The birth order of these patients is shown in figure 2 and is compared with similar data for Tennessee for 1954. The data for white and Negro infants are presented separately. The frequency of anemia in the white infants increased as birth order increased, reaching a peak with the fourth-born infant. A rather different pattern was seen among the Negro infants, with a peak incidence for second-born infants. It is felt that the Negro patients in this group are not a representative sample, and interpretation of this difference will not be attempted.

The weight of the infant at the time his anemia was recognized is plotted against age in figure 3. The 10th, 50th, and 90th percentiles for males are the frame of reference. No race or sex differences are apparent. Premature infants are plotted separately. With five exceptions, the infants under 30 months of age fell below the 10th percentile. Eighty per cent of the premature infants and 37%

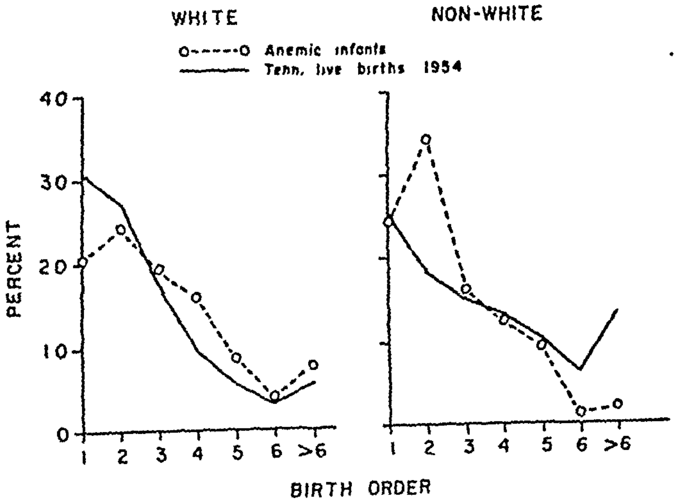

Fig. 2.—Birth order of 174 white and 98 Negro infants with hypochromic anemia compared with that of total live births in Tennessee in 1954.

of the full-term infants fell below the 90th percentile. The weight of the infants over 30 months old have not been included in the figure but have a similar distribution. As a group, these infants appear to be underweight, but not to a degree incommensurate with their small size at birth.

The distribution of hemoglobin concentrations of the sample is given in figure 4. In 41 (15%) of the infants, the hemoglobin was less than 5 Gm. per 100 cc. One infant had a hemoglobin level of 1 Gm. per 100 cc. Sixty per cent of these severely anemic infants weighed less than 2,500 Gm. (5.5 lb.) at birth. No correlation between race, sex, or age and hemoglobin concentration was found.

Twenty-six of the infants in the whole series were twins. Both members of nine pairs were anemic; only one member was anemic in eight instances. Twenty of the twins were premature on the basis of birth weight. In table 3 the incidence of twins is given with the various birth weights, sex, and race groups. In each instance it is higher than would have been expected.

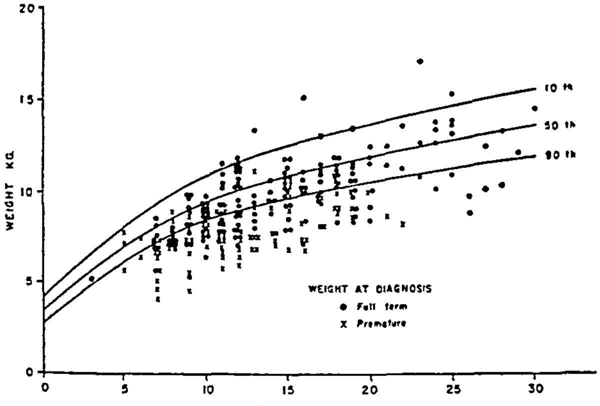

Fig. 3.—Weights of infants with hypochromic anemia occurring under the age of 30 months compared with normal values for white males.

In 25 cases a history of maternal anemia or blood loss during pregnancy was obtained. In only four cases could this information be quantitated. In two of these the maternal hemoglobin concentration was 7 and 8.5 Gm. per 100 cc. at the time of delivery. In two other cases transfusions of the mother had been required. These four infants could not be differentiated from the rest of the group on the basis of any of the parameters studied.

A history of blood loss was obtained in four cases. Two infants had melena and two epistaxis. There were four cases of scurvy. Dysproteinemia was suspected in four infants who had serum albumin concentrations below 2.5 Gm. per 100 cc.

The dietary histories of all the patients were reviewed. The material was not accurate enough for detailed analysis. The most frequent dietary pattern consisted of two quarts of milk daily, usually from a bottle. Those infants receiving any supplement had mashed potatoes, dried beans, crackers, or bread. The diets were characterized by the absence of the iron-fortified cereals, vegetables, eggs, fruits, and meat. A few of the premature infants appeared to be ingesting diets that were adequate. With very few exceptions, prophylactic iron therapy had not been given.

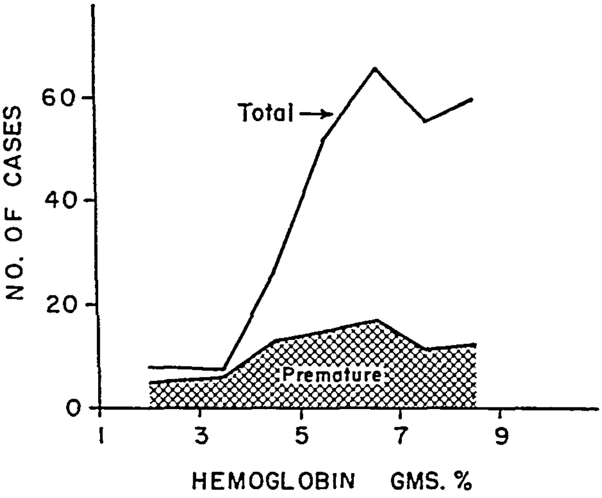

Fig. 4.—Hemoglobin concentration of 272 patients, with separate presentation of premature infants.

There were three deaths among these patients. All occurred within a few hours after admission. One infant had epiglottitis due to Hemophilus influenzae. The other two had pneumonia with cardiac decompensation. In the last two cases it would seem likely that the infants might have survived their infections had they not been anemic.

Comment

The probable causes of iron deficiency in this series of infants will be discussed under the four mechanisms suggested in the introduction, i. e., iron supplies at birth, relative growth rate, available dietary iron, and iron loss.

Table 3.—*Number of Twins in Present Series Subdivided by Race, Sex, and Prematurity Compared with Expected Incidence**

Birth	Race		Twins, No. Found	Twins, No. Expected
Full-Term	White	M	1	0.6
		F	4	0.5
	Negro	M	1	0.4
		F	0	0.1
	Total		6	1.6
Premature	White	M	7	4.3
		F	3	2.7
	Negro	M	8	3.7
		F	2	0.6
	Total		20	11.3

* Duffield and others: Child 5:123, 1940.

Iron Supplies at Birth.—The total body iron at birth may be considered in terms of iron concentration (in milligrams per kilogram of body weight), so that infants of varying birth weights may be compared directly. There is experimental justification for this approach in the data of Widdowson and Spray,[3] who found that the iron concentration during fetal life was relatively constant, with an average value of 75 mg. per kilogram of body weight. The extent of variation from this mean value is not accurately known. Calculations of the iron concentration at birth, based on average values for blood volume and hemoglobin concentration with the addition of an assumed value for tissue stores, are probably less reliable than the actual analyses of Widdowson and Spray. Josephs[4] has recently reviewed this subject and arrived at a normal value of 80 mg. per kilogram of body weight. Variations in such calculations have been discussed by Sturgeon,[2b] who suggested that the total iron level at birth could vary from 129 to 300 mg. in normal, full-term infants. These calculations cover a range of 43 to 75 mg. per kilogram of body weight. The assumption that the iron concentration at birth is normal in infants later developing hypochromic anemia does not rest on any direct evidence. Several recent reports emphasize the variability in iron stores at birth. Kaldor[5] has reported that the iron concentration in the fetal liver is lower in smaller infants. Sisson and Lund[6] have calculated the hemoglobin mass from the plasma volume at 4 or 5 days of age in 25 infants born to anemic mothers and have found a reduction of 3.5 Gm. of hemoglobin per kilogram of body weight, which equals 11.7 mg. per kilogram of iron, or about 19% of the total body concentration of iron. Such differences in hemoglobin mass are large enough to be of critical importance in the infant's iron economy and can exist without the presence of "anemia," as measured by hemoglobin concentration alone. At the present time, it is believed that the circulating hemoglobin mass constitutes the largest iron "store" in the newborn infant.[2a]

Reduction in the iron concentration at birth may occur through either maternal or fetal factors. The maternal factors have been discussed elsewhere.[7] In the present series they are represented by an increased frequency of incidence of anemia in a high birth order and by the four mothers who were anemic at term. In this sample, few cases could be ascribed to maternal factors alone.

The recognized fetal factors operating to reduce the iron concentration at birth are limited to hemorrhage, especially that from the placental circulation. An increasing number of case reports of fetal hemorrhage into the maternal circulation have recently appeared. Fetal exsanguination and shock from acute blood loss in the neonatal period has also received attention. An incidence of 7 cases in 7,400 deliveries was found in this hospital. These cases have threatened the existence of the infants. The number of hemorrhages of similar nature but of lesser degree that have gone unrecognized is unknown. Blood loss in the perinatal period may be a cause of iron deficiency in later infancy.

Evaluation of the possible role of so-called placental transfusion in determining the iron supplies at birth will not be possible until more quantitative data are available.

The special circumstance of multiple births needs to be considered under fetal factors. The frequent occurrence of hypochromic anemia in twins has been recognized for many years. Since twinning occurs with a greater frequency than might be expected in all the race, sex, and birth weight groups in this study, there must be an explanation other than the obvious one of low birth weight. The frequency of abnormal placental circulation is more common in multiple than in single births, especially in single-ovum twins. This is accompanied by an increased incidence of acute blood loss and shock in the neonatal period. The transfusion of one twin by the other can and does occur. Such transfusions could well explain the relatively frequent occurrence of hypochromic anemia in only one of twins when both had similar growth rates and diets. Six twins in this series may well come under this category. Finally, the obvious fact that the twins must divide the available transplacental iron remains as a definite possibility.

The preponderance of male infants in this group, particularly among those born prematurely, is surprising since no reference to an altered sex ratio in patients with iron deficiency has been found. Among premature infants who survive the neonatal period, males constitute the minority group. If the greater mortality among males after the first month of life had been considered in this analysis, the differences would become even more significant statistically. Male infants are less mature than female infants of the same weight as measured by epiphysial ossification[8] and by neonatal mortality.[9] During the course of an investigation of the hemoglobin concentration of infants born to a group of mothers whose nutritional status had been investigated, it was noted that the hemoglobin concentration of male infants was significantly less at the age of 5 to 7 weeks than that of the female infants. Studies of the serum iron concentration in children aged 3-14 years[10] showed lower values among males than among females, a reversal of the situation found in adults. The growth of male infants during the first year of life is greater than that of female infants. On calculating hemoglobin growth on the basis of published values for normal growth and hemoglobin concentration, Drabkin[11] demonstrated increments of 40 Gm. for males and 30 Gm. for females during the first year of life. His calculations indicate that the iron needs of males are greater than those of females during the first year of life. These observations suggest the possibility that sex differences in iron metabolism may occur in infancy as well as in adults. Rachitic tetany and keratomalacia are other nutritional diseases which are known to occur more frequently in males. The preponderance of males in this group of anemic infants is probably related in some way to their relative immaturity as well as to the greater growth rate of males over females.

Relative Growth Rate.—Since the growth rate for large and small infants, as expressed in terms of daily weight gain, remains within relatively narrow limits for both males and females, the main determinant of the relative growth rate is the birth weight itself. The role of low birth weight as a predisposing factor in the development of hypochromic anemia has been documented by Mackay,[12] Davidson and Fullerton,[13] and many others. Despite rather widespread recognition of the fact that premature infants are particularly prone to develop iron deficiency, they still constitute the largest single group of anemic infants from an epidemiologic standpoint. The increased incidence of iron deficiency found in infants weighing 3,000 Gm. (6.5 lb.) or less includes several infants not considered to be immature by more general standards. The most striking observation is the extremely low incidence of severe hypochromic anemia in infants weighing more than 4,000 Gm. (9 lb.). These infants are subjected to the same environmental and dietary factors as the other infants in this series. It must be concluded that their iron needs are less because of a relatively slower growth rate and that their initial total iron supply is greater due to their greater tissue mass.

Dietary Iron.—The dietary iron available could not be estimated from the histories and is unknown in these patients. The fact that they all developed hypochromic anemia is evidence that their iron retention was inadequate. Iron intake considerably in excess of the recommended dietary allowances can easily be achieved.[14] Calculations of the iron needs of infants during the first year of life [2b] suggest that, in some cases, these needs cannot be supplied by ordinary diets. There is little question concerning the fact that diets consisting largely of milk are frequently associated with the development of hypochromic anemia after the age of 6 months.

Iron Loss.—No studies of iron excretion in infants comparable to those done in adults [15] have been carried out. There is no reason to believe that infants conserve iron less well than adults. Occasional cases of hypochromic anemia after blood loss due to trauma or disease do occur. The role of iron excretion in infants as a cause of iron deficiency needs quantitative reevaluation.

Summary and Conclusions

An attempt has been made to determine whether the composition of a group of anemic infants differs from that of the population from which they are drawn. The most significant predisposing factors found were low birth weight, high birth order, twinning, and masculinity. Similar findings were recently reported by Guest and Brown.[16] The poor diets eaten by these infants are similar to those of a much larger number of infants who did not develop anemia of the same degree of severity. Consequently, severe hypochromic anemia in infancy does not occur solely as the result of a deficient iron intake.

Prematurity or a birth weight of less than 3,000 Gm. (6.5 lb.) is the most common predisposing factor. Prematurity was present in 80% of the patients with a hemoglobin concentration of less than 5 Gm. per 100 cc. Reduction of the iron supplies at birth may be due to maternal iron deficiency or fetal blood loss. Unrecognized instances of fetal blood loss may compromise the infant's iron economy without jeopardizing his life. Perinatal hemorrhage may also be an explanation for the high incidence of hypochromic anemia in twins. The more frequent occurrence of hypochromic anemia in male infants is a reflection of their relative immaturity and increased growth rate.

The prevention of hypochromic anemia depends largely on the recognition of the susceptible infants in the population. This group should be given adequate doses of medicinal iron prophylactically and should be carefully watched for the development of anemia.

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Dr. Margaret Martin did the statistical analysis of the data, and Mrs. S. H. Pierce Jr. and Mrs. Willard Faulkner assisted with the compilations.

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URINARY CALCULI

EXCRETION STUDIES AFTER ORAL ADMINISTRATION OF ACETYLSALICYLIC ACID AND GLUCURONOLACTONE

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David Karansky, M.D., Leo Kesner, B.S.
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Though the etiology and pathogenesis of primary calcium urinary stones have not been determined, one possible etiological factor, that of quantitative increase of calcium in urine, appears implicated in many instances. However, the amount of calcium that urine can maintain in solution without precipitation, or its solubility, is unknown.[1] It is generally believed that urine is supersaturated with calcium, as determined by equilibration experiments in which urine of known calcium content is agitated with excess calcium phosphate. If precipitation occurs, calcium goes out of solution, and a supersaturated state is shown to exist; if some of the excess calcium phosphate goes into solution, then a state of undersaturation probably preexisted. Flocks [2] and Andrews [3] found supersaturation common in the urines of stone-forming patients. Hyperexcretion of calcium is thought to be an etiological factor in the increased incidence of urinary stones in recumbency and hyperparathyroidism.

The physical state of calcium in urine has a direct bearing on its solubility. It can be assumed that calcium in urine is present either as free ions in equilibrium with calcium phosphate or held in unionized organic compounds by union with citrates or glucuronides.[4] It is obvious that the greater the amount of calcium held in organic union, the fewer free calcium ions will be available for precipitation and presumably for calculus formation.

Determinations of the factors involved in the solubility of calcium were made before and after the administration of acetylsalicylic acid and glucuronolactone in normal persons and in patients who had formed stones. The pH values of urine did not change after the drugs were administered. There was no alteration of the surface tension after the administration of acetylsalicylic acid or glucuronolactone in normal individuals or those with stones. The administration of acetylsalicylic acid or glucuronolactone did not increase either the total excretion per day or the concentration of calcium and phosphorus per milliliter beyond the range of values that existed before the drugs were given. The concentration of organic acids, such as citrates or glucuronides, in urine also have a direct bearing on the solubility product of calcium phosphate. The administration of glucuronolactone and acetylsalicylic acid in all instances raised the concentration of the glucuronides in urine, but the equilibration experiments as described did not show any direct solvent action of the glucuronides on the calcium in urine at pH 6 and the physiological concentration used.

With this in mind, Prien and Walker [5] have drawn attention to the possible solubilizing effects of glucuronides on calcium in urine. They have

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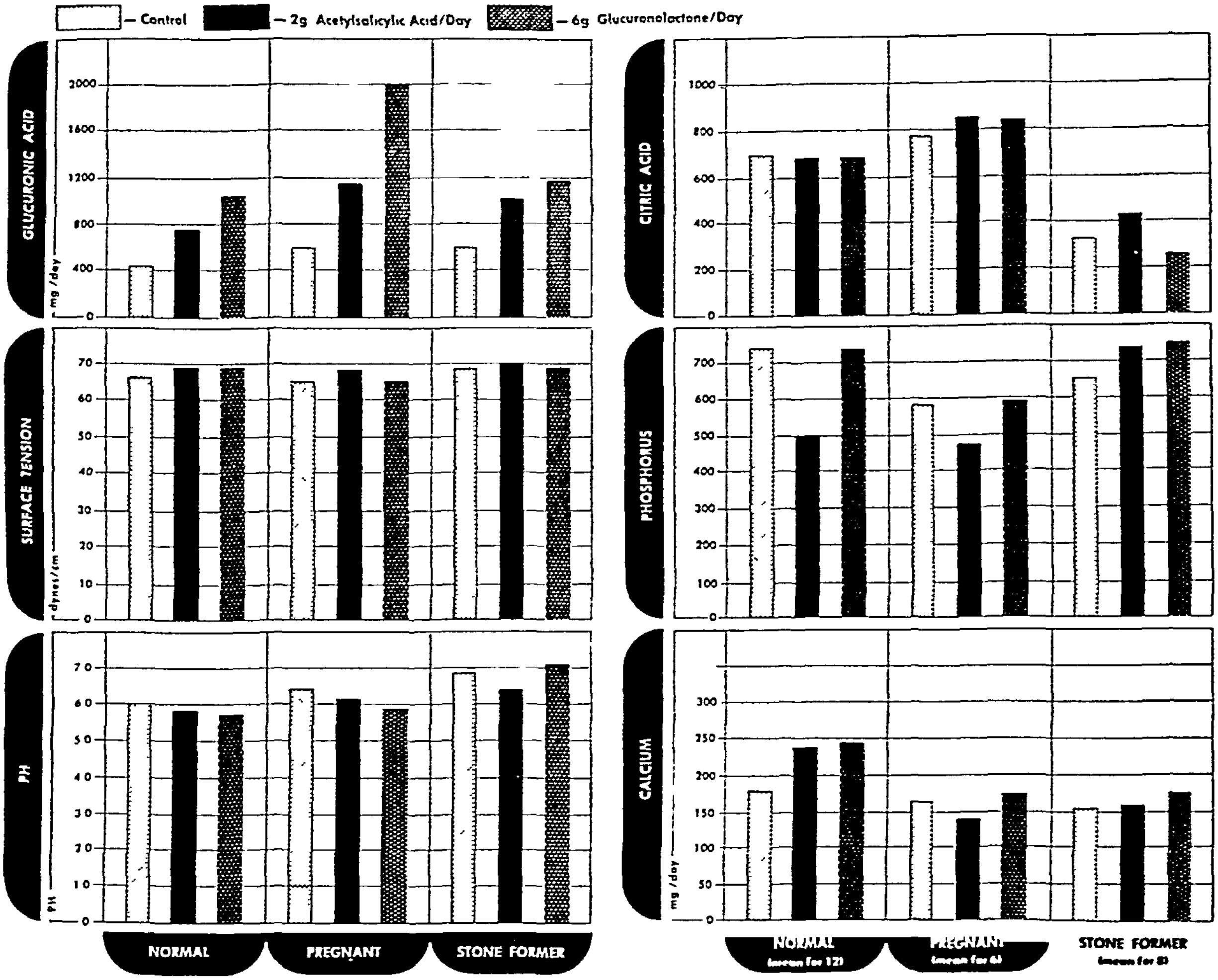
Read before the Forum of Fundamental Surgical Problems at the Clinical Congress of the American College of Surgeons, October, 1957, Atlantic City, N. J.

recommended the administration of acetylsalicylic acid or salicylamide as drugs that can enhance the formation of calcium-glucuronide, a chelated organic union similar to the calcium-citrate complex, and thus prevent the formation and growth of calculi in the urinary tract. This premise is based on experiments by Neuberg and Grauer[6] who showed that the presence of menthol glucuronide in an in vitro solution of calcium chloride and monobasic sodium phosphate can prevent calcium precipitation. However, a 0.139 solution of menthol glucuronide containing 46 Gm. per liter was used, a concentration that cannot be obtained in physiologic solutions. Cessi's[7] work, which followed the studies of Neuberg and Grauer, may also have bearing on the solubility of calcium salts in urine. Cessi's experiments were done with isolated liver slices and demonstrated absorption of tagged tribasic calcium phosphate from physiologic saline solution by the liver slices through the action of the glucuronides. Neutral or slightly alkaline tissue pH is necessary for the formation of an adequate amount of the enzyme glucuronidase which acts as a catalyst for the reaction.

If an analogy can be drawn between the reactions in the liver slices and those in the kidney, then the administration of acetylsalicylic acid and glucuronolactone, which leads to an increased amount of glucuronides in the urine and presumably in the tissues, might alter the concentration or the state of calcium in plasma and perhaps aid in the clearance of calcium. If so, perhaps subjects to whom acetylsalicylic acid, salicylamide, or glucuronolactone was administered might have different amounts of calcium in their urine than before the administration of these drugs. To test this theory, determinations of the factors involved in the solubility of calcium were done before and after the administration of acetylsalicylic acid and glucuronolactone both in normal individuals and in those patients who had formed stones. The determinations were performed in individuals of varying race, age, and sex and in pregnant women. It was hoped



Quantitative evaluation of urinary excretion factors concerned with solubility of calcium in urine of 26 persons.

CLINICAL NOTES

PRURITUS FROM AN UNUSUAL SOURCE—BIRD MITES

REPORT OF A CASE

Milton M. Cahn, M.D.
and
Fred R. Shechter, M.D., Philadelphia

Pruritus is always a distressing symptom and may be provoked by many local or systemic factors; however, at times simple causes may be entirely overlooked. Many patients will suffer with an itch of undiagnosed etiology for many weeks, although a battery of clinical and laboratory studies have been done by numerous physicians. This case is reported because of the unusual and rare source of trouble, namely, a bird mite. Once the etiological diagnosis was established, both patient and physician were gratified with the results of simple therapy.

Report of a Case

A 35-year-old female had nocturnal itching of the face, arms, and legs for eight weeks prior to her first visit to us in August, 1957. The itching soon became generalized, and she experienced a crawling and stinging sensation of her skin. She could identify each "sting" by a small black spot that was present at the site. She developed a few small papules and wheals on her skin. The only relief she could obtain was by taking numerous showers day and night. Her husband, her children, and other members of the household were not affected. She was seen by a number of physicians including internists and dermatologists who, after a survey and numerous laboratory studies (blood sugar, complete blood cell counts, urinalyses, serologic test for syphilis, and liver function studies), came to the conclusion that there was nothing organically wrong but that her symptoms were psychosomatic, the latter strongly coloring this patient's history. She was treated for a number of nonexistent dermatological and medical diseases.

When first seen by us, she had already taken numerous tranquilizers. There is no doubt that we too would have missed the diagnosis if a crawling object on her skin had not been found. Also, several specimens of the "black spots" which annoyed her were removed for study. The crawling object was identified as an Arachnid (4 pairs of legs) (fig. 1) and the black spot, which was brown under the microscope, as excrement of this mite. The Arachnid was then further identified by Dr. E. W. Baker of the United States Department of Agriculture as the northern fowl mite, or Ornithonyssus sylviarum (Canestrini and Fanzago, 1877). With the offender known, a systematic search was made to locate the nests where the mite might live, and success was finally achieved when numerous bird nests infested with these mites were found in a window air-conditioner. This served as a perfect means of dissemination. When the air-conditioner was turned on the mites were blown into the room. The patient's husband, who shared the same room, was never affected. The therapy consisted of removing the air-conditioner, thoroughly cleaning the room, and using general hygienic measures.

Comment

Bird and fowl mites (poultry mites) may reside temporarily on the skin of human beings and cause severe pruritus and dermatitis. Such pruritus may give the patient much mental and physical anguish and the attending physician much harassment. Investigators have reported cases in which such dermatoses have lasted for several years before the cause was discovered.[1] Ticks and mites belong to the class Arachnida. Four pairs of legs are a distinguishing feature. Figure 2[2] represents a classi-

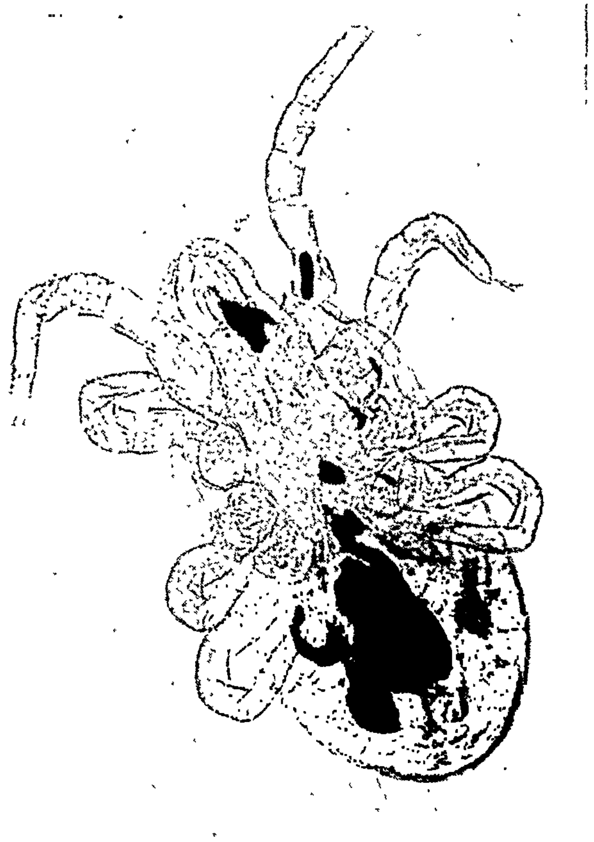


Fig. 1.—Northern fowl mite (Ornithonyssus sylviarum), × 125.

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fication of those mites most commonly found on poultry, one of which was responsible for the symptoms in this case. This constitutes only a small proportion of the kind of mites which are parasitic,[3] since there are numerous families and groups. One of the most important mites is the human itch mite –Sarcoptes scabeii.

Ormsby and Montgomery[4] make many references to the occurrences of bird mite dermatitis. They state that, according to Toomey, bird mite dermatitis was first recognized by Redi in 1684. The Arnolds[5] described a case in which only one of two people sleeping in the same room was affected. This resembled our case, in which no one else in the household was involved although they slept in the same room at various times. Sulzberger and Kaminstein[1] described an eruption with severe pruritus especially at night, caused by mites of infested canaries. Schwartz and his colleagues[6] describe a situation in which many workers in an industrial plant were thought to have an occupational dermatitis. After astute "detective" work, many pigeon nests were located. These were infested with bird mites.

The cutaneous reactions are nonspecific. Eruptions may be papular, vesicular, urticarial, or combinations of these, accompanied by excoriations and crusting. Eruptions may occur on any part of the body exposed to the mites. A fact not generally recognized is that in those people who keep themselves clean, no eruptions may appear. In our case lesions were sparse because the patient bathed frequently, day and night. However, pruritus may be profound even in these cases. Dermatitis caused by bird mites may be confused with scabies because both mites provoke symptoms by seeking refuge in dark places and by attacking the host at night. A very important differential diagnostic point from scabies is that the burrow or cuniculus is absent in bird mite dermatitis.

The particular mite in this case (Ornithonyssus sylviarum) infests birds such as swallows, warblers, and canaries and has been reported to harbor the western equine encephalitis virus. Baker and associates[7] point out that in 1947 investigators in California reported recovery of western equine encephalomyelitis virus from mites taken from the nest of the yellow-headed blackbird, but persistence of infection and transmission by bite were not demonstrated. In 1948 there were reports of further isolation of this virus as well as St. Louis encephalitis virus from specimens of northern fowl mite taken from wild bird nests. Baker also states that under experimental conditions Newcastle disease (pneumoencephalitis) was recovered from northern fowl mites that had fed upon sick chickens, but the virus did not persist in the mites.

The significance of the chicken mite (Dermanyssus gallinae) as a possible vector for human disease has also increased recently since the demonstration that it may be a natural vector of eastern equine encephalitis,[8] although there are many references to dispute this.[9] The common chigger (red bug, harvest mite) is capable of causing skin damage in man, and several species are important as vectors of tsutsugamushi fever. Finally, two other animal mites should be mentioned, namely, the tropical rat mite (Ornithonyssus bacoti), a blood-sucking parasite of rats which transmits the rickettsia of endemic typhus, and the mouse mite (Allodermanyssus sanguineus), which transmits the agent of rickettsialpox.

These fowl mites do not reside on the human skin but are merely temporary visitors. Therefore, our patient received no benefit from various antiparasitic treatments applied to the skin. Nor did any of these measures prevent the mites from biting. The only treatment of help was the removal of the source, the infested bird nests. Then a plain soap and hot water bath was sufficient to cure the patient.

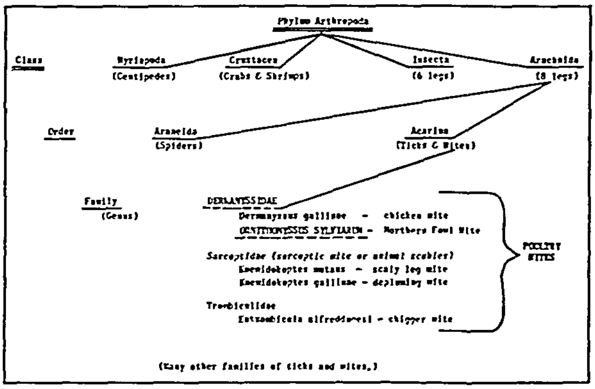
Phylum Arthropoda
Class
Myriapoda
(Centipedes)
Crustacea
(Crabs & Shrimps)
Insecta
(6 legs)
Arachnida
(8 legs)
Order
Araneida
(Spiders)
Acarina
(Ticks & Mites)
Family
(Genus)
DERMANYSSIDAE
Dermanyssus gallinae - chicken mite
ORNITHONYSSUS SYLVIARUM - Northern Fowl Mite
Sarcoptidae (sarcoptic mite or animal scabies)
Knemidokoptes mutans - scaly leg mite
Knemidokoptes gallinae - depluming mite
Trombiculidae
Eutrombicula alfreddugesi - chigger mite
POULTRY MITES
(Many other families of ticks and mites.)

Fig. 2.–Classification of poultry mites.

The control of poultry mites is discussed in a leaflet issued by the United States Department of Agriculture[2] and by Baker and associates.[7] For the control of the northern fowl mite, one of the medicaments they recommend is an insecticide containing malathion, as a dust or spray. They also stress that directions must be carefully followed for most effective use.

Summary

A woman had severe pruritus and mild dermatitis caused by bird mites. The cause was found to be the northern fowl mite (Ornithonyssus sylviarum). A window air-conditioner harbored numerous bird nests infested with this mite. The patient had been extensively studied and was labeled neurotic before the source of the pruritus was found.

Mites may cause dermatitis which is sometimes severe or sometimes insignificant. Animal mites may be the vectors of serious systemic disease. While bird mites are an unusual cause of pruritus, they should be considered in the differential diagnosis, especially when the patient does not respond to routine therapy.

1930 Chestnut St. (3) (Dr. Cahn).

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TRIETHYLENETHIOPHOSPHORAMIDE IN TREATMENT OF METASTATIC CEREBRAL MALIGNANCY

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Diabetes insipidus should be considered a symptom. It is usually chronic, but it may be acute and temporary. The case to be reported exemplifies the chronic, secondary type of diabetes insipidus. It was due to metastatic cancer to the pituitary stalk; it was occult but suspected of being malignant and treated as such because of a lack of therapeutic responses with the usual modalities.

Report of a Case

A 68-year-old female had been suffering for six months from diabetes insipidus, diagnosed elsewhere. The lack of response to therapy with vasopressin (Pitressin) tannate in oil and inhalations of posterior pituitary powder as a snuff was responsible for reference to our clinic for evaluation. She had weighed 142 lb. (64.4 kg.) when the symptoms began; she was 62 in. (157.5 cm.) tall and weighed 100 lb. (45.4 kg.) when seen by us. She stated that, for several months before and continuously after the symptoms began, she had vague and occasionally severe pain in the left upper portion of the abdomen and under the ribs in the left lower side of the back. She could, at times, get relief by lying on her abdomen or bending forward. A complete neurological and physical examination was negative except for obvious dryness of the mucous membranes and skin. There was some tenderness on deep pressure over the left upper lateral border of the left side of the rectus muscle and in the left part of the hypochondrium. There were no masses or organ enlargements palpable. Roentgenographic studies of the skull and of the abdominal organs failed to reveal any abnormalities.

Blood and urine chemistry studies were negative. The specific gravity of the urine varied from 1.001 to 1.003. The total daily fluid intake was from 7 to 8 gal., but the urinary output was from 8.5 to 9 gal. daily. Dehydration was becoming progressively worse. Intravenous administration of a hypertonic solution of saline and glucose, inhalations of posterior pituitary powder, injections of vasopressin in oil, and administration of 600 mg. of aminopyrine orally four times daily did not alter the course of the disease.

An intravenous injection of a 2.5% hypertonic saline solution at a rate of 0.25 cc. per kilogram of body weight per minute for 45 minutes showed an increase in the flow of urine, tending to confirm the absence of an antidiuretic hormone. A presumptive diagnosis of occult, metastatic carcinoma to the supraoptic region from a cancer in the tail of the pancreas was made. This diagnosis was suggested because of the abdominal and back pain which was relieved by the prone position or forward bending and because it had preceded and continued after the start of the symptoms of diabetes insipidus.

Accordingly, 40 mg. of triethylenethiophosphoramide (Thio-TEPA) was injected into the right common carotid artery in the same manner used in angiography. There was no untoward reaction. In three days improvement was noted, and in nine days the patient had gradually returned to what appeared to be a normal physiological state. She remarked that the abdominal discomfort was less.

After the ninth day the patient returned to normal and remained well for 5 months and 21 days, with a weight gain to 121 lb. (54.9 kg.). Gradually, she noted a return of increasing thirst, dryness of her mouth, and increasing urination. There was a slight response to therapy with vasopressin in oil if it was given four times daily. This time, 40 mg. of triethylenethiophosphoramide was given in the left common carotid artery. A favorable response began in 4 days and was complete in 11 days. For the next 3 months and 19 days she felt well, but after this she again began taking vasopressin in oil because she felt she needed it. She had been trained, as with a diabetic, to give herself the injections. She kept herself comfortable with vasopressin injections from one to three times weekly for the next two months. She became totally refractory, and 50 mg. of triethylenethiophosphoramide was injected into the right

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carotid artery. A remission started in 4 days, but it lasted only for 28 more days. She was given 3,600 r (in air) with use of a 250-kv. machine and a 5-cm. cone. In 10 days a partial remission occurred, which lasted for three more weeks. She became progressively weaker and died.

Postmortem examination revealed a 1-cm. carcinoma of the tail of the pancreas densely adherent posteriorly, but there were no evidences of local metastases. There was a 4-mm. metastasis in the pituitary stalk in the region of the hypothalamic supraoptic nuclei. The tracts had been transected by it. There had been no interference with cerebral fluid dynamics.

Comment

In 1943 and 1951, nitrogen mustard was used in intracarotid injections for treatment of metastatic cerebral malignancy in two cases. One was metastatic carcinoma of the maxillary sinus, and the other was metastatic cancer of the lung. In both instances the convulsions and unconsciousness that followed the injection were as dramatic as the improvement, which lasted three and five months respectively. Nitrogen mustard was not used in this case because of the profound cortical effects witnessed previously. However, the results probably would have been as good.

Summary

An occult cancer of the tail of the pancreas metastasized to the pituitary stalk, causing symptoms of diabetes insipidus. The response of this patient to intracarotid administration of triethylenethiophosphoramide was unusual. Intracarotid administration of nitrogen mustard, used previously in two similar cases, was not attempted because of possibility of profound cortical effects.

Addendum

During the life of the patient reported on and since this paper was submitted, eight patients with cerebral metastases from cancer of the breast and three with cerebral metastases from cancer of the lung have been treated by intracarotid injections of triethylenethiophosphoramide (Thio-TEPA). All were unconscious at the time of initial treatment. Full lucidity and consciousness was regained from four to six hours after the injection. Within six days there was a return of normal activity. In 11 months of use of this therapy, only one patient died; this occurred six months after the first treatment, and autopsy revealed cancer in the brain. All of the remaining patients are alive with cancer. Remissions have been maintained by repeated intracarotid injections of the drug every seven to nine weeks. Local skin metastases respond to local injections into the tumor.

The triethylenethiophosphoramide used in this study was supplied as Thio-TEPA by Dr. James Ruegsegger of the Lederle Laboratories Division, American Cyanamid Co., Pearl River, N. Y.

SPECIAL ARTICLE

A STUDY OF CERTAIN NONPOLIOMYELITIS AND POLIOMYELITIS ENTEROVIRUS INFECTIONS

CLINICAL AND SEROLOGIC ASSOCIATIONS

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Recently the term "enteroviruses" was introduced as descriptive of a large group of human viruses which includes the three polioviruses, the Coxsackie viruses, and the ECHO viruses.[1] These agents have many properties in common, including the ability to multiply in the human gastrointestinal tract with or without the production of clinical disease. Disease, when it does occur, most frequently involves the central nervous system (CNS). Classification of the enteroviruses into the three groups listed above has become more difficult as certain properties originally believed unique for one group are found to be shared by others. Further evidence of common pathogenic and serologic properties are presented in this communication.

Numerous nonpoliomyelitis enteroviruses have been associated with aseptic meningitis, a subject recently reviewed by others.[2] A few paralytic illnesses have also been reported which were associated with nonpoliomyelitis enterovirus infections,[3] and some in combination with a poliovirus.[4] Present data indicate that Coxsackie A-7,[5] ECHO-2,[5c] ECHO-6,[6] ECHO-9,[7] and some Coxsackie B [8] viruses may cause paralytic illness resembling poliomyelitis clinically. This report contains further

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evidence that certain other members of the Coxsackie and ECHO groups may or actually do cause mild paralysis.

Six paralytic cases from the gamma globulin field trials of 1952[9] are discussed, the etiologies of which have been examined as thoroughly as possible. In addition, 10 nonparalytic poliomyelitis-like illnesses (aseptic meningitis) and five healthy individuals, each infected with a nonpoliomyelitis enterovirus, are described. The latter five infections, together with some of the others, show a broad serologic response by complement fixation which suggests minor antigenic relationships between certain nonpoliomyelitis and poliomyelitis enteroviruses.

Materials and Methods

Cell Culture.—Monolayer cell cultures of trypsinized rhesus monkey kidney were used in isolation studies, neutralization tests, and preparation of complement-fixing antigens. Prior to December, 1956, medium 199 was used as fluid phase. By this time it was evident that lactalbumin hydrolysate in Earle's balanced salt solution with 0.5% calf serum generally maintained cell cultures and supported viral multiplication as well as did medium 199, possessed greater buffering capacity, and was more economical to prepare. Mediums employed prior to October, 1956, contained 400 units of penicillin and 0.2 mg. of streptomycin per milliliter. Thereafter 20 units of polymyxin and 25 units of nystatin (Mycostatin) were also added to each milliliter.

Virus Isolation.—The methods employed for the laboratory examination of the specimens from the gamma globulin field studies of 1952 have been described previously.[9b] Fecal specimens or rectal swabs obtained from patients of the 6208th U. S. Air Force Hospital at Clark Air Force Base (CAFB) in the Philippine Islands were tested for virus in the same manner. Viruses were identified in neutralization tests with antiserums specific for Coxsackie, ECHO, and polioviruses. Materials from which an ECHO virus was isolated were also tested for Coxsackie viruses in day-old suckling mice through three blind passages.

Serology.—Neutralizing antibody (NA) tests were performed on all serums from one subject simultaneously. Fourfold dilutions beginning at 1:4 were employed. Equal volumes of virus, 100 tissue culture infective doses ($TCID_{50}$) per 0.1 ml., and serum dilution were mixed and incubated one hour at room temperature; 0.2 ml. was added to each of two monkey kidney cell cultures. Control titrations of each virus were performed simultaneously to determine the actual test dosage. Results were expressed as the reciprocal of that serum dilution calculated by the method of Reed and Muench[10] to protect 50% of the inoculated cell culture tubes.

Poliovirus complement-fixation (CF) tests were carried out by a modification[11] of the Fulton and Dumbell plate method[12] with use of heat-inactivated cell culture antigens which had been prepared by the concentration technique described by Svedmyr, Enders, and Holloway.[13] Results are expressed as the reciprocal of the highest serum dilution which gave a 2+ reaction in the presence of two units of complement and two units of antigen. Antigens were prepared and the majority of CF tests were performed prior to February, 1955.

Clinical Diagnosis.—Paralytic cases which occurred during the gamma globulin field studies were classified quantitatively on the basis of graded muscle weakness. A detailed account of this method of scoring and its applications was reported previously.[9a] A clinical diagnosis of paralytic disease was accepted only when there were characteristic physical findings and history together with definite weakness of one or more muscles in the absence of pain, muscle spasm, or other explanatory cause. Muscle involvement data reported herein represent the degree of residual muscle weakness at the 60-day examination. The highest possible score in the event of complete paralysis of all muscles was 560. A diagnosis of nonparalytic poliomyelitis (aseptic meningitis) was made only in the presence of positive cerebrospinal fluid findings, associated with clinical manifestations and a typical history. The basis for the clinical diagnosis of nonparalytic poliomyelitis or aseptic meningitis in patients from CAFB was obtained from abstracts of clinical records forwarded from the Philippines.

Laboratory Diagnosis.—Quantitative poliovirus NA and CF tests were made on all serum specimens. In the absence of a significant NA rise to any of the three polioviruses, all tests were repeated. In those instances in which a nonpoliovirus was isolated and serum was available, NA tests were performed against the virus isolated. With serums of patients from CAFB, NA tests were also carried out against ECHO 1, 12, and 13 and Coxsackie A-9 viruses. These agents had been shown in a previous study by Hammon and co-workers[14] to be producing infections in this area. Hemagglutination-inhibition tests with Japanese B encephalitis, mumps, and influenza viruses as well as CF tests against the virus of lymphocytic choriomeningitis were occasionally included in the serologic examination of CAFB patients. These latter four tests were carried out at the U. S. Army's 406th Medical General Laboratory in Japan.

Final laboratory diagnosis was based on virus isolation and confirmation of serologic data when available. In the absence of a virus isolation, an increase in NA titer of fourfold or greater was considered significant and indicative of infection, as was an increase from <1:4 to 1:8 or more. CF rise alone was not accepted as diagnostic for poliomyelitis since heat-inactivated cell culture antigens occasionally gave titer rises in instances in which all other data indicated that no poliovirus infection had occurred. Several others [15] have reported similar findings.

Findings

Paralytic Cases Without Poliovirus Infection.—No laboratory evidence of a poliovirus infection was found in three patients whose illnesses could not be differentiated clinically from paralytic poliomyelitis. In each instance a Coxsackie virus was isolated. A significant serologic response was demonstrated to the virus isolated in two cases examined (table 1). All three cases are described below.

Iowa-53.—During the first week after the onset of a paralytic illness Coxsackie B-4 virus was isolated from the feces of this 4-year-old boy, who had been inoculated with gelatin placebo. A serum specimen taken on the fourth day revealed the presence of NA to types 1 and 3 polioviruses but not to the virus isolated (table 1). Two additional specimens, obtained approximately five and nine weeks later, showed no significant change in poliovirus serology, whereas a significant NA increase, from <1:4 to 1:32, occurred to the Coxsackie B-4 virus during the first five weeks of illness.

TABLE 1.—*Cases of Clinical Paralytic Poliomyelitis-like Disease Without Evidence of Concurrent Poliovirus Infection but Associated With Coxsackie Virus Isolation*

						Serology†							
						Polioviruses							
			Virus Isolation			1		2		3			
Area and Case	Age and Sex	60-Day Muscle Score	Type	Day*	Day of Serum Specimens*	NA	CF	NA	CF	NA	CF	NA to Virus Isolated	Etiology Laboratory Methods
					4	16	<4	<4	4	256	32	<4	
Iowa 53	4 M	4.75	Coxsackie	5-7	35	8	<4	<4	8	128	16	32	Coxsackie
			B-4		60	8	<4	<4	8	128	16	..	B-4
					2	<4	<4	<4	<4	<4	<4	64	
Iowa 102 .	2 F	16.5	Coxsackie	3-6	32	<4	<4	<4	<4	<4	<4	256	Coxsackie
			B 3‡		68	<4	<4	<4	<4	<4	<4	64	B 3
					2	1,024	8	<4	<4	<4	<4	...	
Texas 197 ..	4 M	3.0	Coxsackie	3,10	31	2,048	8	<4	<4	<4	<4	...	Coxsackie
			A 9§		60	2,048	8	<4	<4	<4	<4	...	A 9

* Day specimen obtained after onset of illness
† NA = neutralizing antibody, CF = complement fixing antibody
‡ Also isolated from one well sibling
§ Also isolated from two well siblings

These results indicate that this individual had had a previous experience with type 1 and 3 polioviruses and that the present illness was probably the result of the Coxsackie virus infection.

Iowa-102.—During the first week of paralytic illness a Coxsackie B-3 virus was isolated from the feces of this 2-year-old noninjected girl and also from her 3-year-old gelatin-injected healthy sister. The NA and CF titers of all three serum specimens collected from both girls, 2, 32, and 68 days after onset of illness in the patient, were less than 1:4 to all three types of poliovirus (table 1). Serologic studies on the healthy sibling are not shown. In contrast with the poliovirus serology, both girls showed a fourfold NA rise and fall to their respective B-3 viruses.

These serologic findings show that this illness could not be attributed to a poliovirus infection. The only apparent conclusion is that this disease was the result of the Coxsackie B-3 infection.

Texas-197.—The third patient was a 4-year-old noninjected male from whom Coxsackie A-9 virus was isolated early in the paralytic disease. Although a high NA titer, 1:1,024, and a CF titer of 1:8 to type 1 poliovirus were present at onset, no significant serologic changes to any of the three polioviruses occurred during the following two months. Coxsackie A-9 virus was also isolated at the same time from two healthy siblings of the patient. Their poliovirus serology was identical with that of the patient. No poliovirus was isolated from either of these children. Because of repeated serologic tests with polioviruses, all serum specimens were exhausted and could not be tested against the A-9 virus isolated.

There remains little doubt that the A-9 infection and disease were related and that the type 1 poliovirus antibodies were evidence of an earlier experience with that virus.

Paralytic Cases Probably Without Poliovirus Infection.—Three paralytic patients from whom no poliovirus could be isolated demonstrated suspicious poliovirus CF findings without significant changes in NA during the two months after onset of illness. In each instance an ECHO virus was isolated and a serologic response (NA) demonstrated to the isolated virus (table 2).

Iowa-97.—Type 16 ECHO virus was isolated from a pool of feces of this 11-year-old gamma globulin-inoculated paralyzed girl. The feces were collected between the sixth and ninth day after onset. A serum sample taken on the fifth day contained NA to all three polioviruses, but not to the virus isolated. The second specimen taken a month later neutralized ECHO-16 virus in a dilution of 1:8 while poliovirus NA titers did not change. However, the CF titers to all three polioviruses rose eightfold to sixteenfold during this interval. This latter observation is suggestive of the CF group reaction which is commonly found with heat-inactivated poliovirus antigens during some poliovirus infections, especially when the current infection has been preceded by experience with one or more polioviruses.

Whether the CF rise in Iowa-97 was caused by the ECHO-16 virus infection cannot be determined. The lack of a rise or fall in NA titers to any of the three polioviruses, their relatively modest titers, and our failure to isolate a poliovirus suggest that the CF rise was not the result of a current poliovirus infection. Further instances of the CF group reaction will be noted later.

The evidence that this paralytic disease was the result of the ECHO-16 infection is not conclusive. However, ECHO-16 has been shown to produce meningeal pleocytosis in monkeys after intrathecal injection,[16] and in man it has been associated with aseptic meningitis and an exanthem.[17] It is of interest to note that gamma globulin failed to protect this child against the CNS disease probably caused by ECHO-16.

Texas-123.—During the first week of illness ECHO-4 virus was isolated from the stool of this gamma globulin-inoculated 3-year-old boy, as well as from the feces of a well sibling. NA and CF antibodies to all three types of poliovirus were present in relatively low titer at the onset of illness while no NA was found for ECHO-4 virus. Two additional serum specimens, which were obtained at consecutive four-week intervals, showed only a twofold rise in type 2 poliovirus NA titer followed by a fourfold fall; these variations are within the possible range of error of the method. CF antibodies to all three polioviruses were present but showed no significant changes. On the other hand, ECHO-4 NA increased from <1:4 to 1:16 and then receded to 1:4.

The above serologic findings together with the isolation of only ECHO-4 suggest strongly that this paralytic illness was the result of the ECHO-4 infection. ECHO-4 has not been associated previously with paralytic illness; however, it has been isolated from patients with aseptic meningitis and exanthem.[18] So far, extensive studies on the neurotropic properties of ECHO-4 in other primates have not been reported. As in the previous case, gamma globulin did not afford protection.

Table 2.—*Cases of Clinical Paralytic Poliomyelitis-like Disease with Doubtful Evidence of Concurrent Poliovirus Infection but with ECHO Virus Isolation*

			Virus Isolation			Serology†							
						Polioviruses							
						1		2		3			
Area and Case	Age and Sex	60-Day Muscle Score	Type	Day*	Day of Serum Specimens*	NA	CF	NA	CF	NA	CF	NA to Virus Isolated	Etiology: Laboratory Methods
					6	128	<4	8	8	128	32	<4	
Iowa-97	11-F	1.0	ECHO	6-9	37	128	16	8	128	128	256	8	ECHO
			16		60	128	8	8	64	64	256	8	16
					1	32	32	8	16	64	16	<4	
Texas-123	3-M	3.0	ECHO‡	3-4	30	32	16	16	16	64	8	16	ECHO
			4		57	32	16	4	16	128	8	4	4
					4	64	64	<4	16	128	32	8	
Texas-175	3-F	2.5	ECHO	4-7	37	64	16	<4	8	128	16	128	ECHO
			4		64	64	8	<4	<4	128	8	<10	4

* Day specimen was obtained after onset of illness.
† NA = neutralizing antibody; CF = complement-fixing antibody.
‡ Also isolated from a well sibling.

Texas-175.—The third case in this section is similar to the preceding one. ECHO-4 virus was isolated from the feces of this 3-year-old gelatin-injected girl during the latter portion of the first week of illness. NA to polioviruses types 1 and 3 and CF antibodies to all three types were present in a serum specimen taken on the fourth day after onset. At this time, the NA titer for the homologous ECHO-4 virus was 1:8. Nearly five weeks later the ECHO-4 NA titer had risen to 1:128, whereas no changes were noted in poliovirus NA levels. During this same interval, CF titers to all three polioviruses decreased twofold to fourfold and, as shown in table 2, continued to decline at about the same rate for the next four weeks. During this latter interval the ECHO-4 NA titer receded to <1:10.

Herein is another example of a poliovirus CF group reaction, the cause of which cannot be determined with certainty. Whether the CF changes were related to the ECHO-4 infection and accompanying immunological response is not known. A similar CF finding was not noted in the preceding ECHO-4 infection, Texas-123. The findings in both Texas-123 and Texas-175 are evidence that ECHO-4 may cause paralytic illness.

Cases of Aseptic Meningitis Associated with Nonpoliomyelitis Enterovirus Infections.—As a result of virus isolation and serologic studies, we have selected for presentation 10 patients with aseptic meningitis who were found to be infected with a nonpoliomyelitis enterovirus. Three of the cases selected, Texas-31, Texas-192, and Iowa-123, were from the gamma globulin field trial. Texas-31 had received gamma globulin. The remaining seven were patients at CAFB, Philippine Islands. In five instances, a nonpoliomyelitis enterovirus was isolated from fecal material (table 3). Three isolations of ECHO-4, one in the child given gamma globulin and one each of ECHO-3 and Coxsackie B-4, were made. In the five remaining individuals (table 4) extensive serologic tests revealed the presence of two Coxsackie A-9 infections; two of ECHO-1, one of which occurred in conjunction with an ECHO-12; and one of ECHO-13.

In serums from 9 of the 10 patients no significant increase in poliovirus NA titers occurred during the course of illness. In the 10th patient, CAFB-DJ, NA titers to types 1 and 2 poliovirus rose to only 1:8 and fell promptly to the original <1:4 level, a serologic finding not characteristic of true poliovirus infection.

Serums from Iowa-123 from whom ECHO-4 was isolated during the acute phase of illness (table 3) gave persistent, relatively high poliovirus type 1 (ca 1:2,048) and, to a lesser degree, type 3 (ca 1:256) NA titers, while CF titers to all three polioviruses were falling during the observation period (table 3). These findings suggest that either a type 1 poliovirus infection preceded the ECHO-4 infection or that the latter infection elicited a serologic response in the form of a poliovirus CF group reaction. Even though this illness occurred during a poliomyelitis type 1 outbreak,[19] it seems reasonable to believe that ECHO-4 was etiologically involved because only ECHO-4 was isolated and it has been formerly associated with aseptic meningitis.[20]

A poliovirus group CF response also occurred in CAFB-SJ who, as shown in table 4, gave serologic evidence of a simultaneous infection with ECHO viruses 1 and 12. In this latter connection a pool of ECHO-12 hyperimmune monkey antiserums prepared by Dr. Herbert Wenner [1b] has been found to neutralize ECHO-1 virus in dilutions one-hundredfold less than the homotypic end point. The converse has not been found, and similar results have not been obtained with lower titered ECHO-12 antiserums. In view of the above findings, which have been confirmed in at least three other laboratories, it appears improbable that the appearance of NA to ECHO-1 in CAFB-SJ was the result of only an ECHO-12 infection. Furthermore, in three other ECHO-12 infections studied, one of which is shown in table 5 as 2-85, a significant serologic response to ECHO-12 was not accompanied by an increase in NA titer to ECHO-1. Although it is likely that dual infection with ECHO viruses 1 and 12 occurred in CAFB-SJ, the cause of this illness cannot be established since there are three etiological possibilities—ECHO-1 alone, ECHO-12 alone, or both together.

Nonpoliovirus Infection in Healthy Individuals.—Table 5 presents the results of tests for viruses and of the serologic examinations of five healthy individuals found to be infected with a nonpoliomyelitis enterovirus. These individuals were selected from the longitudinal survey of American families in the Philippines [14] to further illustrate the appearance of an occasional CF reaction to heat-inactivated poliovirus antigens during the immunological response to another enterovirus.

In one instance a 2-year-old girl, 1-163, who had had an earlier experience with type 1 poliovirus, was found to be infected with ECHO-4 and Coxsackie B-3 and B-4. Each of these three viruses was isolated in sequence and neutralizing antibodies to each were developed. A significant rise in types 2 and 3 poliovirus CF antibodies was demonstrated even though no NA to either type was detected during the observation period (table 5). The CF antibody rise was associated in time with the ECHO-4 infection and antibody response. Two other individuals, 1-186 and 2-47, from whom ECHO-1 was isolated, exhibited concurrent increases in NA to ECHO-1 and CF antibodies to type 3 poliovirus. In neither instance was there any evidence of NA to any of the three types of poliovirus. A fourth person, 2-85, who was infected with ECHO-12, showed an increase in ECHO-12 NA from <1:4 to 1:128 and concurrently fourfold to eightfold increases in CF antibodies for all three polioviruses. The serologic response of 2-86, who was also infected with ECHO-12, was similar to that of the sibling 2-85, except that no change was noted in the CF titer to type 1 poliovirus. Both 2-85 and 2-86 exhibited no significant change in type 2 poliovirus NA titers, the only type to which NA was demonstrated.

Comment

Initially this discussion will be concerned with the six paralytic illnesses which apparently were not due to a poliovirus infection (tables 1 and 2).

TABLE 3.—*Cases of Aseptic Meningitis and Results of Laboratory Studies for Etiology*

		Virus Isolation			Serology†							
					Polioviruses							
					1		2		3			
Area and Case	Age and Sex	Type	Day*	Day of Serum Specimens*	NA	CF	NA	CF	NA	CF	NA to Virus Isolated	Etiology: Laboratory Methods
Texas-31	4-M	ECHO-4	8-11	6	<4	<4	<4	<4	<4	<4	<4	ECHO-4
				58	<4	<4	<4	<4	<4	<4	8	
Iowa-123	4-M	ECHO-4	1,8	2	2,048	>256	<4	128	512	64	Serum exhausted	ECHO-4
				27	4,096	64	<4	64	256	32		
				60	1,024	32	<4	16	256	16		
CAFB-ER	23-M	ECHO-4	2	2	512	<4	8	4	128	4	Serum exhausted	ECHO-4
				15	128	...	8	...	64	...		
CAFB-RC	7-M	ECHO-3	17	12	512	<4	<4	8	<4	<4	Serum exhausted	ECHO-3
				47	512	<4	<4	4	<4	<4		
Texas-192	3-M	Coxsackie B-4	9-11	9	256	<4	<4	<4	<4	<4	16	Coxsackie B-4
				36	128	<4	<4	<4	<4	<4	128	
				64	128	<4	<4	<4	<4	<4	64	

* Day specimen was obtained after onset of illness.
† NA = neutralizing antibody; CF = complement-fixing antibody.

It should be emphasized that these illnesses had been diagnosed as clinical paralytic poliomyelitis by a team of experienced poliomyelitis clinicians engaged in a research evaluation.[9a] We refer to these illnesses now as paralytic poliomyelitis-like because there is essentially no laboratory evidence of a poliovirus infection. This distinction is made because of the formerly held concept that this type of paralytic disease is only caused by one of the three types of poliovirus.

Whether the enteroviruses isolated in all six cases were the respective etiological agents is not unequivocally established. The fact that virus was isolated from the feces during the acute phase of illness and its presence was followed, in the five cases in which the serums were tested, by a significant serologic response to the virus isolated, establishes the temporal relationship between onset of infection and onset of disease.

In the past, the demonstration of a poliovirus infection during the acute phase of illness, as established by isolation of the virus from the feces or by serological means, has been accepted as diagnostic. This acceptance was based on the knowledge that these viruses infect the intestinal tract of man, produce a typical pathology in fatal cases, and produce similar pathology in other primates when infected experimentally. With the exception of Coxsackie B-3,[21] none of the five enteroviruses involved in these paralytic illnesses has been reported to produce fatal CNS disease in man. Thus, human CNS pathology as a result of infection with four of these viruses, ECHO-4, ECHO-16, and Coxsackie A-9 and B-4, is not known. Furthermore, experimental paralytic disease has not been reported in primates with these five viruses. This may be attributed in part to the lack of adequate testing with a large number of strains. For example, after the "Russian Poliovirus Type 4"[3b] was identified as a Coxsackie A-7, Habel and Loomis[3a] found that two American strains of Coxsackie A-7 also produced "CNS lesions identical with severe poliomyelitis" in monkeys when inoculated intracerebrally. Coxsackie B-3 has been reported by Kibrick and Benirschke[21] as having produced CNS lesions in the spinal cord and the myocardium of one infant who died of the disease.

Other strains of ECHO-4 and ECHO-16 and Coxsackie A-9, B-3, and B-4 have been isolated from patients with aseptic meningitis and are acknowledged etiological agents of this syndrome.[22] It seems justifiable to expect instances in which the combination of unusual viral invasiveness and/or host susceptibility results in progression of the disease with the involvement of motor neurons as in poliomyelitis. In other words, there may exist strains of enteroviruses which, with opportune conditions, act like polioviruses in man and produce an occasional paralytic illness that clinically cannot be differentiated from paralytic poliomyelitis. We feel that these six cases are examples of the occasional paralytic illness caused by a nonpoliomyelitis enterovirus. Others, previously reported, were cited above.

Ten cases of aseptic meningitis were described which were associated with nonpoliomyelitis enterovirus infections. These viruses were ECHO types 1, 3, 4, 12, and 13 and Coxsackie A-9 and B-4. Only ECHO viruses 1, 12, and 13 have not been associated by others with CNS disease. However,

TABLE 4.—*Cases of Aseptic Meningitis and Results of Laboratory Studies for Etiology*

Area and Case	Age and Sex	Virus Isolation		Day of Serum Specimens*	Serology†								Etiology: Laboratory Methods
					Polioviruses								
					1		2		3				
		Type	Day*		NA	CF	NA	CF	NA	CF	Other Virus NA		
											ECHO-13		
CAFB-MJ	11-F	None	2	3	<4	<4	<4	8	64	4	8		ECHO-13
				16	<4	<4	<4	8	64	<4	32		
				42	<4	<4	<4	16	64	<4	8		
											Coxsackie A-9		
CAFB-DJ	23-M	None	6	4	<4	<4	<4	4	16	<4	16		Coxsackie A-9
				18	8	<4	8	16	8	8	64		
				48	<4	<4	<4	16	16	8	64		
											Coxsackie A-9		
CAFB-BG	22-M	None	3	5	<4	...	128	...	<4	...	64		Coxsackie A-9
				20	<4	...	128	...	<4	...	256		
											ECHO-1		
CAFB-QW	20-M	None	2	2	8	<4	<4	16	16	16	32		ECHO-1
				15	4	4	<4	32	32	32	1,024		
				54	4	<4	<4	32	16	32	128		
											ECHO-1	ECHO-12	
FB-SJ	27-M	None	7	2	64	<4	<4	8	16	<4	<4	<4	ECHO-12 and ECHO-1
				14	128	8	<4	32	8	8	16	32	
				54	128	4	<4	16	8	8	4	4	

* Day specimen was obtained after onset of illness.
† NA=neutralizing antibody; CF=complement-fixing antibody.

Hammon and co-workers [14b] previously pointed out suggestive evidence of the etiological role of ECHO-1 and ECHO-12 in connection with another group of patients. Thus the list of viruses which are probably involved in CNS disease becomes even longer and the evidence of etiology more convincing.

These paralytic and nonparalytic illnesses cannot be expected to be prevented by the present poliomyelitis vaccine and may be considered vaccine failures unless the exact etiology is established. Three of these were also noted as gamma globulin failures. The laboratory results reported herein emphasize the importance of complete etiological study of paralytic and nonparalytic poliomyelitis-like disease.

Considerable CF work has been performed in the past with heat-inactivated poliovirus antigens. Our experience with this type of preparation has been extensive over a number of years, over 4,000 tests having been performed. These antigens have proved useful, but frequently the results have been difficult to interpret. Not only did they occasionally give evidence of a CF group reaction in the presence of a poliovirus infection but also occasionally demonstrated a significant poliovirus CF reaction in the absence of a poliovirus infection but in the presence of another enterovirus infection. Ten out of many instances of a poliovirus CF response in the presence of another nonpoliomyelitis enterovirus infection have been presented. The viruses involved included ECHO types 1, 4, 12, and 16 and Coxsackie type A-9. It may be suggested that what we have demonstrated is merely an anamnestic reaction mediated by the infecting virus. This possibility cannot be overlooked in the eight instances in which NA was present to one or more polioviruses at the onset of illness. However, in two "triple negatives" who were infected with ECHO-1 (table 5) this concept is much less tenable. It seems more likely that the CF responses observed in all 10 cases resulted from minor antigenic relationships between these nonpoliomyelitis and poliomyelitis enteroviruses which are apparently demonstrated only by CF reactions with heat-inactivated poliovirus antigens. It should be noted that three of these reactions occurred during infection by ECHO-4. Further studies should be made of this phenomenon. Unfortunately animal experiments have not proved to be appropriate means, since the group antigenic relationship even between polioviruses has been demonstrable only in man.

At present the serologic associations demonstrated here lend strong support to the concept of common antigens between poliomyelitis and nonpoliomyelitis enteroviruses as revealed by this type of CF procedure, thus justifying its continued use to acquire more such data. However, it is obvious that heat-inactivated monkey kidney cell culture antigens are not satisfactory when the CF test is used alone for the specific diagnosis of poliomyelitis. Several other more specific antigens are now available for this latter purpose, but because of their greater type specificity, their use cannot be expected to throw more light on the intriguing problem of common antigens.

It becomes more apparent through these series of patients and normal persons presented above that two properties which up to recently have been considered unique for polioviruses, at least insofar as the enterovirus group was concerned, are shared by the Coxsackie and ECHO viruses. The first of

Table 5.—*Serologic Studies of Five Healthy Persons Infected with Nonpoliomyelitis Enteroviruses*

					Serology†								
					Polioviruses								
		Virus Isolation			1		2		3		NA to Virus Isolated		
No. of Case	Age and Sex	Type	Day*	Day of Serum Specimens*	NA	CF	NA	CF	NA	CF	E-4	B-3	B-4
		ECHO-4	59	0	1,024	<4	<8	8	<8	<4	<2	<4	<4
1-163	2-F	Coxsackie B-3	67	59	...	<4	<8	64	<8	32	8	<4	<4
		Coxsackie B-4	118	118	1,024	<4	<8	64	<8	16	>256	16	32
				0	<4	<4	<4	<4	<4	<4		16	
1-186	3-M	ECHO-1	44	56	<4	<4	<4	<4	<4	8		>256	
			121	121	<4	<4	<4	<4	<4	8		128	
				0	<4	8	<4	16	<4	16		<4	
2-47	29-F	ECHO-1	28	28	<4	8	<4	16	<4	32		4	
				84	<4	8	<4	32	<4	64		64	
				0	<4	8	64	16	<4	16		<4	
2-85‡	6-M	ECHO-12	14	28	<4	32	...	128	<4	64		128	
				84	<4	8	128	16	<4	8		32	
				0	<4	<4	128	8	<4	<4		<8	
2-86‡	3-F	ECHO-12	28	110	<4	<4	128	>16	<4	16		128	

* Collection day after first serum specimen.
† NA=neutralizing antibody; CF=complement-fixing antibody.
‡ Siblings (2-85 and 2-86).

these properties is paralytic disease manifestations illustrated here by six cases, and the second is antigenic constitution, as demonstrated by serology in at least 10 instances. No claim is made that any single case or normal person in this series presents conclusive evidence of pure infection by a single ECHO or Coxsackie virus and that the disease occurring or the serologic findings were the result of such single infection. However, it is considered probable that such is the case for the majority. This evidence, together with previous data summarized from a variety of sources, supports these conclusions. This raises a question regarding the justification for continuing to call members of the enteroviruses by three different generic-like names, as more and more of their bases for original definition and classification are found to be shared rather than confirmed as distinct or unique.

Summary

Laboratory studies on the etiology of 6 paralytic poliomyelitis-like illnesses and 10 cases of aseptic meningitis established essentially no evidence of poliomyelitis virus infection, by either isolation or serologic methods. The probable etiological agents of the paralytic illnesses were shown to be Coxsackie viruses A-9, B-3, and B-4 and ECHO viruses 4 and 16. Gamma globulin failed to protect against the central nervous system disease apparently produced by ECHO-4 and ECHO-16 viruses. The viruses associated with aseptic meningitis were Coxsackie types A-9 and B-4 and ECHO types 1, 3, 4, 12, and 13.

In five of the above illnesses attributed to ECHO or Coxsackie viruses serologic studies revealed the presence of a CF response to heat-inactivated monkey kidney cell culture poliomyelitis antigens. Similar findings were presented for five healthy individuals, also infected with nonpoliomyelitis enteroviruses. It is suggested that these immunological responses are the result of minor common antigens. The viruses apparently eliciting this response in man included Coxsackie type A-9 and ECHO types 1, 4, 12, and 16. It is concluded therefore that certain ECHO and Coxsackie viruses not only overlap with polioviruses in their pathological effects on the central nervous system, in a manner believed formerly to be essentially unique for polioviruses, but also they bear antigenic relationships to polioviruses. Thus, these three groups of agents become less distinct and become progressively more difficult to define and justify as members of separate generic-like classifications.

130 DeSoto St., Pittsburgh (13) (Dr. Hammon).

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. Kautz, M.D., *Secretary.*

CURRENT STATUS OF THERAPY IN ANEMIAS

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Anemia, like any other useful sign of disease, is most efficiently corrected when therapy is directed at the specific pathological process or deranged physiological mechanism responsible for its development. The administration of a blood transfusion is the only direct treatment for anemia. It is effective in elevating the hemoglobin concentration, although often only temporarily, in a wide variety of disease states, even when it is employed without regard to the pathogenesis of the anemia. This is somewhat similar to the indication for an alcohol sponge bath for the patient with excessively high fever or the use of tracheotomy for acute laryngeal edema. All are useful, sometimes lifesaving, direct therapeutic attempts to relieve an abnormal sign of disease without altering the causative factors.

Anemia is usually defined as the state in which there is found a reduction in the concentration of hemoglobin, the number of erythrocytes, or the volume of packed red blood cells in a specific quantity of the circulating blood. The mean values for these measurements found in healthy adult males, adult females, and children of various ages differ significantly, as indicated in table 1.

No single value can be used, therefore, as a standard of reference ("100% level") for hemoglobin concentration, red blood cell count, or hematocrit for all individuals. Thus, many "slight anemias" of females are seen to be spurious when the hemoglobin values are judged in the correct frame of reference.

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enterally. They relate total dose of iron to the weight of the patient and his initial hemoglobin concentration.

Saccharated iron oxide (Proferrin) is another form of iron available for parenteral use. This is given intravenously, diluted in saline solution, at doses of 50 to 100 mg. per injection, to adults. Smaller amounts are recommended for children. Since its wide use during the past several years, it has been demonstrated to be more effective and far less toxic than earlier intravenously administered iron preparations had been. However, as with all forms of iron given parenterally, a regular incidence of toxicity occurs which requires one to exercise extreme care with each administration. Perhaps more important is the necessity for a compelling indication for the use of this form of therapy as opposed to oral treatment. These indications in an adult include a malabsorption syndrome, making oral therapy with iron preparations ineffective, and extreme sensitivity of the gastrointestinal tract to iron salts because of intrinsic disease or idiosyncrasy.

TABLE 5.—*Disorders Associated with Megaloblastic Anemia*

Disease	Effective Therapeutic Agents
Pernicious anemia	Cyanocobalamin
Nutritional macrocytic anemia	Cyanocobalamin in some cases and folic acid in others
Sprue, idiopathic steatorrhea	Cyanocobalamin and/or folic acid
Total gastrectomy	Cyanocobalamin
Intestinal strictures, blind loops	Surgical correction, broad-spectrum antibiotics, cyanocobalamin, folic acid
Diphyllobothrium latum infestation	Cyanocobalamin
Megaloblastic anemia of infancy	Folic acid, ascorbic acid
Megaloblastic anemia of pregnancy	Folic acid
Tropical macrocytic anemia	Folic acid and/or cyanocobalamin
Achrestic anemia	Folic acid

Another cause of microcytic hypochromic anemia is thalassemia. In this hereditary disorder there exists a congenital defect in erythropoiesis. Inadequate numbers of red blood cells are produced, and those that are found are abnormal. They vary a great deal in size and shape; many target cells and small fragmented erythrocytes (schistocytes) are seen as well as normoblasts and stipple cells. Since the survival time of these cells in the circulation is shortened, two factors are present to account for the anemia: inadequate production and excessive hemolysis. At times, there occurs in these patients the complicating factor of an extracorpuscular hemolytic state which offers an additional therapeutic challenge. In this disease, in spite of the resemblance to iron deficiency anemia, administered iron is not beneficial and actually may be harmful. Iron stores are usually excessive. It is the utilization of the available iron which seems to be disturbed.

The treatment for thalassemia is symptomatic. Transfusions are administered when the hemoglobin level falls below a critical point at which symptoms of anemia become manifest. Although this varies widely in individual children with this disease, in general, a hemoglobin value of less than 7.0 Gm. per 100 ml. of blood is the usual indication for transfusion. It is not practical to attempt to maintain the hemoglobin at normal levels by transfusion and actually is harmful. Not only is the risk of transfusion reaction and serum hepatitis increased, but the large numbers of transfusions required only seem to speed up the development of hemosiderosis and finally of hemochromatosis, which develops eventually in patients with thalassemia major and which is the ultimate cause of death in many of these children. In selected instances, splenectomy has been found to be effective in thalassemia when an extracorpuscular hemolytic anemia exists.

Macrocytic Anemias

For this discussion, an anemia is classified as macrocytic when the mean corpuscular volume is greater than 94 cu. μ. These anemias can be divided into two large groups: (1) those associated with megaloblastic erythroid precursors in the bone marrow and (2) those associated with normoblastic erythroid precursors. The megaloblastic anemias form a large group of entities with the following common characteristics: macrocytic normochromic erythrocytes, megaloblastic erythropoiesis, leukopenia, thrombocytopenia, and dramatic therapeutic response to specific antianemic preparations. Depending upon the pathogenesis of the disorder, such preparations include cyanocobalamin, folic acid, and ascorbic acid.

Pernicious anemia and related disorders are usually readily diagnosable when patients are seen in hematological relapse. A diagnosis of pernicious anemia, sprue, and megaloblastic anemia incident to total gastrectomy demands therapy for the remainder of the life of the patient. A definitive diagnosis therefore should be established before therapy is undertaken, since partial remission induced by suboptimal therapy can make the diagnosis difficult to establish. Table 5 includes a list of the different disorders often associated with megaloblastic anemia and the usually effective therapeutic agents.

Pernicious Anemia.—For patients in relapse, cyanocobalamin is the drug of choice in this disease. It is administered intramuscularly in doses of about 30 mcg. daily until a good hematological response is observed, usually for about two weeks. If the number of reticulocytes has not risen within the first 10 days, the correctness of the diagnosis should be suspected. Within two weeks the hemoglobin level, hematocrit, and red blood cell values should rise considerably. The percentage of increase is usually proportional to the severity of the anemia prior to therapy; that is, greater gains will be made in the more anemic patients. After two weeks the dose may be reduced to 30 mcg. given once or twice per week. Maintenance therapy is required for the life of the patient and may be adequately carried out with 45 to 60 mcg. of cyanocobalamin injected intramuscularly at intervals of four to six weeks. When severe combined systemic disease (posterolateral sclerosis) is found, it is recommended that a larger dose of cyanocobalamin be given at more frequent intervals.

Liver extract is equally effective in pernicious anemia when administered in comparable dosage; i. e., one unit of liver extract is equivalent to one microgram of cyanocobalamin. There is no real evidence that liver extract has any more value in this disease than can be accounted for by its cyanocobalamin content. Since it is more painful to inject, allergic reactions do occur in some patients; and since larger volumes are required for comparable cyanocobalamin content, it is not as desirable as cyanocobalamin.

Oral administration of cyanocobalamin alone is ineffective, because the basic defect in pernicious anemia is the absence of gastric intrinsic factor required for its absorption. Exceptionally large oral doses (3,000 mcg.) are capable of inducing remission, but the expense of this form of therapy precludes its use.

Cyanocobalamin, combined with potent intrinsic factor from animal sources, can be used orally to induce remission and can maintain patients in good health for long periods. This form of therapy is not yet considered as reliable as parenteral therapy with cyanocobalamin alone because of a wide variation in the potency of various intrinsic factor concentrates and because of the uncertainty of the stability of some of these preparations when stored. For these reasons, at this time such therapy is not considered suitable for routine use.

Folic acid is contraindicated in pernicious anemia, and iron is required only when a combined iron deficiency exists. However, folic acid is indicated for the treatment of megaloblastic anemia of pregnancy, megaloblastic anemia of infancy, some cases of sprue, nutritional megaloblastic anemia, tropical macrocytic anemia, and refractory megaloblastic anemia. The usual dose is 5 to 20 mg. daily, administered orally. Parenterally administered preparations, such as sodium folate (Sodium Folvite), are available for use in infants or in adults too ill to tolerate oral therapy. In the megaloblastic anemias of infancy and pregnancy, therapy is usually indicated until hematological remission is induced, and then it may be stopped without relapse occurring. In sprue and nutritional megaloblastic anemias, the administration of folic acid may be required for long periods and sometimes indefinitely.

Macrocytic Anemias Without Megaloblastosis

Macrocytic anemias without megaloblastosis form a heterogeneous collection of disorders usually secondary to some primary disease not localized to the hematopoietic system. In chronic liver disease, which is the most common cause, the erythrocytes are large and often very thin so that increased numbers of target cells are seen. Chronic blood loss is frequent in cirrhosis of the liver, probably as a result of bleeding from esophageal varices, hemorrhoids, or peptic ulcerations. As a result, macrocytic hypochromic cells are found. Iron therapy will partially influence the hemoglobin values beneficially. The underlying liver failure is in some way responsible for most of the hemoglobin deficit, however, and this is refractory to therapy directly with any of the known hematinics.

Scurvy.—When scurvy is severe enough, it may be associated with a macrocytic anemia reputedly, in some instances, associated with megaloblastic erythropoiesis. Ascorbic acid is the specific agent in the treatment of this disorder. In this instance, leucovorin (citrovorum factor) theoretically may have a specific role in the treatment of anemia, since ascorbic acid depletion is associated with a decrease in the conversion rate of folic acid to citrovorum factor.

Anemia of Myxedema.—In the endocrine deficiency, myxedema, anemia is frequently found. The erythrocytes may be microcytic hypochromic (probably when associated with menorrhagia in females), normocytic normochromic, or macrocytic. The use of thyroid or its active principles for the treatment of the underlying hypothyroidism is frequently effective in restoring blood values to normal. Iron may be required in the depleted individual.

Normochromic Normocytic Anemias.—For this discussion, an anemia is classified as normocytic normochromic when the mean corpuscular volume is 82 to 92 cu. μ and the mean corpuscular hemoglobin concentration is 32 to 36%. The anemias found in this morphologic category include almost all types of anemia not already discussed.

Acute Blood Loss.—When severe hemorrhage occurs, the degree of anemia, as depicted in the peripheral blood cell counts at any one moment, is dependent upon a variety of factors. Some of these include (1) the amount of whole blood lost, (2) the original size of the vascular space, (3) the alterations which have occurred in the size of the vascular compartment, i. e., vascular contraction or expansion, (4) the amount of plasma or red blood cell regeneration, and (5) shifts in the intravascular localization of blood from one area to another, i. e., splanchnic pooling or peripheral vasoconstriction.

The hemoglobin concentration or the volume of packed red blood cells obtained from a sample of peripheral blood, therefore, will not necessarily directly reflect the total amount of blood loss. Immediately after a hemorrhage the blood values may be normal. As plasma is replaced into the vascular space, even though bleeding has ceased, the values will progressively fall for as long as 12 to 24 hours. If circulatory collapse occurs, hemoconcentration may occur, and blood cell counts may rise.

Therapy for hemorrhage includes transfusion of whole blood to replace the volume lost and measures directed at correcting the bleeding. There is no substitute equal to whole blood transfusion for the treatment of hemorrhage. Normal human plasma is used only when blood is not available, as a temporary measure to maintain circulating volume. Ideally the transfused blood should be antigenically similar to that of the recipient in regard to major group and Rh type. Crossmatching should always be performed to eliminate the possibilities of incompatibilities not detected otherwise. For the patient who has had transfusions previously, the extra precaution of employing the indirect Coombs crossmatching method is considered worth the additional effort. Even when relatively mild, the reaction which follows in the wake of an incompatible transfusion can be disastrous for the patient who is under the physiological stress of acute hemorrhage.

Hemolytic Anemias.—Although each of the many types of hemolytic anemia occurs infrequently, the category, as a whole, is a sizable one. It is beyond the scope of this presentation to review the pathogenesis and therapy for each of the disease states associated with an excessive rate of erythrocyte destruction. Some generalizations are possible, however. All the hemolytic anemias may be considered to fall into two groups: those associated with an abnormality intrinsic in the erythrocyte as it is developed (intracorpuscular defect) and those in which the primary defect is an abnormality present in the environment of the erythrocyte, which then alters the viability of the normally produced cell (extracorpuscular defect).

The four basic measures employed in the management of hemolytic anemias include (1) administration of corticotropin (Acthar, Corticotropin, Depo-Acth) or adrenal cortical steroids, (2) splenectomy, (3) transfusion, and (4) removal of any adverse environmental factors.

Adrenal Steroid Therapy: Adrenal steroid therapy, as typified by the administration of corticotropin, cortisone (Cortisone, Cortogen, Cortone) acetate, and prednisone (Deltasone, Deltra, Meticorten), is of great value in the management of the extracorpuscular hemolytic anemias. The types most often benefited include the idiopathic, acquired hemolytic anemias with and without demonstrable antibodies, the symptomatic hemolytic anemias (those associated with malignant lymphomas, chronic lymphocytic leukemia, collagen diseases, and miscellaneous tumors), and the hemolytic states resulting from drug sensitivities. The dosage of corticotropin usually employed is 25 to 50 U. S. P. units given intramuscularly every six hours. It may be used intravenously as well. A dosage of 25 to 50 units of corticotropin, dissolved in a liter of isotonic sodium chloride solution and administered by slow drip over a period of 16 to 20 hours, may produce a rapid therapeutic response. Cortisone, in quantities up to 300 mg. per day, or prednisone, in amounts up to 100 mg. per day, is occasionally required to halt the hemolytic process in refractory cases. Usually less is required. When a response is noted, that is, when hemoglobin values rise and the indications of hemolysis disappear, the steroid dosage may be decreased slowly. A gradual weaning process is often necessary in the patient receiving adrenal steroids. The patient should be carefully observed for recurrence of hemolysis when low levels of medication are reached. Often, prolonged maintenance therapy is required at a daily dose level which varies with each patient but which should be just adequate to prevent hemolysis.

Splenectomy: Splenectomy is resorted to in patients with acquired hemolytic anemias when adrenal cortical steroids either prove ineffective or are contraindicated for some reason. In patients with hereditary spherocytosis with anemia, it is the treatment of choice. In this disorder, the hemolytic anemia is uniformly benefited, although the basic intracorpuscular defect persists. In the uncomplicated case of thalassemia or sickle cell disease, splenectomy is of no benefit. However, there are certain instances of these diseases in which transfusion requirements are excessive and in which an extracorpuscular hemolytic mechanism, which is superimposed upon the basic disease, can be demonstrated. It is only in these patients with thalassemia and sickle cell anemia that splenectomy may be beneficial.

Transfusions: Transfusions are administered to all patients with hemolytic anemia when the number of circulating erythrocytes falls to very low levels. Usually an absolute indication for blood transfusion is the finding of the hemoglobin concentration below 7.0 Gm. per 100 ml. Coronary artery disease, myocardial failure, or rapid hemolytic rates may require the use of transfusion sooner. Great caution must be exercised when administering a transfusion to patients with acquired hemolytic anemia who have autoantibodies. Occasionally, panagglutinins are present which make proper crossmatching and typing of blood extremely difficult. At times the transfusion of packed red blood cells or saline-washed erythrocytes reduces the incidence of reactions.

Removal of Adverse Environmental Factors: The removal of adverse environmental factors is the fourth measure employed in the treatment of hemolytic anemia. This refers particularly to the acquired hemolytic anemias when the pathogenesis is known. The chemotherapy of malaria or the antibiotic treatment of septicemia is, of course, the method of choice in the treatment of the hemolytic anemias associated with these diseases. It is of value to remember that the presenting sign of a disease such as subacute bacterial endocarditis may be hemolytic anemia. When a chemical agent can be implicated in the pathogenesis of hemolytic anemia, its removal from the internal or the external environment of the patient may be all that is necessary to effect a cure. Industrial exposure to naphthalene, trinitrotoluene, benzene, nitrobenzene, aniline, lead, and methyl chloride and medicinal exposure to sulfonamides, quinine, pamaquine, primaquine, and aminosalicylic acid (*p*-Aminosalicylic Acid, Pamisyl, Para-Aminosalicylic Acid, Para-Pas, Parasal, Propasa) have been implicated not infrequently in the production of hemolytic anemia. A complete medical history, taken with especial emphasis on any such industrial, household, or pharmacological exposure, is often the most important potentially therapeutic step that can be taken by the attending physician. There is no evidence to suggest that cyanocobalamin, liver extract, folic acid, or any other vitamins have any specific therapeutic benefit in the management of hemolytic anemia. Iron is not necessary, since the iron liberated by the hemolyzed erythrocytes is not lost from the body and is readily available for new hemoglobin production. The one exception to this is in the management of patients with hemolytic anemia associated with chronic hemoglobinuria, such as paroxysmal nocturnal hemoglobinuria. In this disorder, enough hemoglobin and its associated iron may be lost in the urine to necessitate supplementation with iron salts.

Anemias Due to Bone Marrow Hypofunction

For this discussion, an anemia due to bone marrow hypofunction is a disorder in which the red blood cells are usually normochromic and normocytic. The causes for bone marrow hypofunction can be considered in five groups: (1) chemical or physical injury of marrow, (2) invasion of marrow by nonhematopoietic cells, (3) metabolic interference with erythropoiesis, (4) hormonal factors, and (5) idiopathic hypofunction (table 6).

Except for the use of splenectomy in hypersplenism and hormonal replacement in endocrine deficiency states, no specific treatment exists for the anemia present in this collection of disorders. When an underlying disease such as chronic infection or lymphoma is responsive to direct therapeutic measures, the anemia will respond simultaneously. Supportive measures such as transfusion have value in the severely anemic person. A dose of 50 mg. of cobalt chloride daily has been used with some success. Although its exact mode of action is unknown, cobalt seems to behave as a stimulant to erythropoiesis. It is potentially toxic and is often poorly tolerated, causing nausea and diarrhea. Although some rise in red blood cell counts may follow its administration, subjective deterioration is frequent and its use has to be abandoned. The known hematinics such as iron, folic acid, cyanocobalamin, and liver extract have no value in this group of diseases.

Table 6.—*Anemias Due to Bone Marrow Hypofunction*

- Chemical or Physical Injury to Marrow
  - Irradiation
  - Radioactive substances
  - Nitrogen mustards
  - Thiourea compounds
  - Benzene
  - Heavy metals
  - Sulfonamides
  - Chloramphenicol
  - Phenylbutazone
- Myelophthisis Due to Presence of Abnormal Tissue in Marrow
  - Metastatic neoplasms
  - Multiple myeloma
  - Lymphoma
  - Leukemia
  - Lipoidosis
  - Osteosclerosis
  - Myelofibrosis
- Metabolic Inhibition
  - Uremia
  - Infection
  - Chronic liver disease
  - Malignancy
- Hormonal Factors
  - Hypersplenism
  - Hypopituitarism
  - Hypothyroidism
- Idiopathic Hypofunction
  - Refractory anemia
  - Aplastic anemia

Summary

Anemia is not a disease but a designation given to a laboratory finding present in almost all chronically ill patients and in many whose illness is of short duration. When possible, therapy is directed at the underlying disease. This implies the necessity for a precise diagnosis. Often, careful analysis of the blood by the judicious use of clinical laboratory methods is of great assistance in arriving at a diagnosis and thereby the selection of effective therapeutic agents.

vascular compartment, i. e., vascular contraction or expansion, (4) the amount of plasma or red blood cell regeneration, and (5) shifts in the intravascular localization of blood from one area to another, i. e., splanchnic pooling or peripheral vasoconstriction.

The hemoglobin concentration or the volume of packed red blood cells obtained from a sample of peripheral blood, therefore, will not necessarily directly reflect the total amount of blood loss. Immediately after a hemorrhage the blood values may be normal. As plasma is replaced into the vascular space, even though bleeding has ceased, the values will progressively fall for as long as 12 to 24 hours. If circulatory collapse occurs, hemoconcentration may occur, and blood cell counts may rise.

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ORGANIZATION SECTION

THE FORAND BILL

Recently there was issued from the American Medical Association a booklet entitled "Facts About the Forand Bill." This booklet lists 15 questions with answers. In addition, Dr. David B. Allman, President of the American Medical Association, on April 4, mailed to members of the A. M. A. a letter in which he commented on the Forand Bill HR 9647. Since then, Aime J. Forand has written to Dr. F. J. L. Blasingame, commenting on the A. M. A. leaflet and Dr. Allman's letter. For the readers of The Journal, *the leaflet, Dr. Allman's letter, and Representative Forand's letter are reproduced.*—Ed.

Facts About the Forand Bill

1. Q. *What is the Forand bill?*

A. The Forand bill, H. R. 9467, is an AFL-CIO sponsored amendment to the present Social Security Act. The bill proposes to provide government hospital and surgical care for approximately 13 million eligible social security claimants, principally persons over 65. The bill was introduced in the House in August 1957 by Rep. Aime J. Forand (D., Rhode Island). It was referred to the House Ways and Means Committee of which Forand is the third ranking member. The committee is expected to begin hearings in May.

2. Q. *In brief, what would the Forand bill do in the field of health care?*

A. Bring the aged and other Old-Age Survivors Insurance claimants under government-supervised health care. The government would make contractual agreements to reimburse hospitals, nursing homes, physicians and dentists for specified services rendered to the 13 million (1958) social security claimants (expected to be as many as 22 million by 1975). Payments would be made directly to hospitals, physicians and nursing homes. No payments would be made to individual claimants.

3. Q. *What would the health care proposals cost all workers?*

A. There is no way of accurately predicting the cost. It could prove so costly that it would jeopardize the retirement security of millions of Americans who depend on social security for their basic retirement needs. For the first time last year the social security system received less income than it paid out. Taxes to finance the present program are already scheduled to reach 8½% of payroll up to $4,200 in coming years. The Forand bill provides for raising the social security tax base from the first $4,200 of income to the first $6,000. The tax rate would also be increased ½ of 1% for both employers and employees and ¾ of 1% for self-employed persons. This increase, in addition to those already provided by the social security law, would mean that a self-employed person could be paying $427.50 in social security taxes by 1975.

4. Q. *Would this raise in the social security tax cover the cost of the program?*

A. Possibly at its inception. However, other countries with similar socialistic health programs have found that their costs were several times larger than the original estimates. It is most likely that the Forand bill program would eventually cost much more than two billion dollars per year and that the taxes woud have to be raised accordingly.

5. Q. *What are the basic faults of the Forand bill in the field of health care?*

A. The Forand bill proposes a political solution to a health problem. It is a health care bill developed by non-medical people (chiefly the AFL-CIO).

6. Q. *Would the Forand bill adversely affect health care for the rest of the population?*

A. Over-utilization of hospitals by social security claimants would limit the number of beds available for the acutely ill of all ages in the community. Provisions for extensive free hospitalization would create needless and dangerous crowding of hospital space. In many countries where similar legislation is in effect, there has been a staggering increase in use of hospital facilities by those over 65. (In Saskatchewan, Canada, for example, the average person over 65 occupies a hospital bed 7.2 days a year; in the United States the average person over 65 occupies a hospital bed 2.5 days a year.)

7. Q. *Could all doctors, hospitals and nursing homes participate?*

A. No. Only those that enter into contracts with the government. Furthermore, except in an emergency, surgery could be performed only by a surgeon certified by the American Board of Surgery or one who is a member of the American College of Surgeons. Elective surgery is not included. Care would not be authorized in a mental or tuberculosis hospital. Nursing homes would (1) have to be operated in connection with a hospital or (2) operated under the general direction of a licensed doctor or surgeon.

8. Q. *Who would determine fees for doctors and charges for hospitals and nursing homes?*

A. The Federal Department of Health, Education and Welfare would make the final determination.

9. Q. *Who would administer this program and set standards of care?*

A. The program would be administered by the Secretary of Health, Education and Welfare. The government would set and enforce standards of health care under bureaucratic control.

10. Q. *What hospital and nursing home services would be provided by the Forand bill?*

A. The bill provides a combined total of 120 days free hospital and nursing home care but with a maximum of 60 days hospitalization. However, before a person can receive nursing home care he must be transferred there from a hospital for further treatment of the same illness.

11. Q. *Are any other services provided by the Forand bill?*

A. Oral surgery would be provided, but only to those persons who were hospital bed patients. Oral surgery is not defined.

12. Q. *What effect would the Forand bill have on voluntary health insurance?*

A. The health insurance industry has proved its ability to handle the extensive insurance needs of our growing population. Because of its experience and success in other fields, it is reasonable to allow it time to solve this additional problem—medical coverage for our citizens in the 65-and-over group. Approximately 50% in this age bracket has some coverage now, as compared to only 20% in 1950. Passage of the bill would give voluntary health insurance a set-back from which it would never recover. This bill would do irreparable harm to the one method through which our older citizens can take care of their health needs on a free-choice basis, maintaining full independence. Under the Forand bill the aged would become, in effect, wards of a bureaucratic system.

13. Q. *How do the uninsurable receive health care?*

A. The 3.5 million or so, 65 or over, who are uninsurable because of inadequate income, assets, or other means of support generally receive medical care through welfare programs. Aside from aid granted by many private, fraternal, and religious organizations, over three billion dollars in federal and state aid is given annually to those in the four categorical aid programs (aid to the blind, handicapped, dependent children, aged) for medical and other expenses.

14. Q. *How good are the statistics on the health problems of the aged?*

A. AMA has studied the available statistics. They have been found to be neither conclusive nor complete. The greatest need right now is for a comprehensive study of the health problems of the aged, rather than for drastic remedies for a situation about which so little is known.

15. Q. *Could the age limit for Forand health care be held at 65?*

A. Probably not. Supporters of the bill have indicated that they would like to see government-regulated health care made available to younger persons, perhaps first starting at age 60, then 55, and so on, eventually bringing everyone under a government dictated health program. Ultimately the practice of medicine in America would be totally socialized, which could result in an inferior grade of health care.

American Medical Association
April 4, 1958

Dear Doctor:

A bill now in Congress would place the health care of the aged and other OASI claimants under government supervision.

The Forand bill—H. R. 9467—would provide government hospital and medical care for about 13 million social security claimants by amending the Social Security Act. The AFL-CIO sponsored this bill and has given it top legislative priority.

The Forand bill is not in the public interest. There are several basic reasons why it is bad legislation for all Americans. These are:

1. It would bring the aged under government controlled and supervised health care. The government would set and enforce standards of health care under bureaucratic control, limiting the choice of hospitals and physicians.
2. It would eventually destroy private health insurance and the Blue Shield-Blue Cross plans.
3. It would introduce into the economy of the country, on a permanent basis, wage, fee and price fixing by government fiat.
4. It is national compulsory health insurance for a segment of our population. Once established, this concept would be extended to all social security claimants. Ultimately America would have nationalized hospitals and medical care for everyone.
5. It is an attempt to solve a complicated health problem by political means rather than through established medical resources. Making the aged wards of the government with health care handouts is not the proper way to solve the problem.
6. It would mean higher taxes and less take-home pay for all wage earners for the benefit of a minority.
7. It could bankrupt the entire social security program and jeopardize the basic retirement incomes of millions of Americans.

Every physician must be prepared to oppose this bill vigorously and be ready to make his views known to the Congress should that become necessary.

So that you may be acquainted with this ill-conceived piece of legislation, the A. M. A. has prepared the enclosed pamphlet.

Meanwhile, some of the most important and respected organizations in the health field are preparing a program which will lead toward solution of the problems of health care for the aged. Announcement of this constructive plan will be made soon and details of the program will be supplied to you.

Your active support may be needed for legislative activities which will be carried out by state and county medical societies as required by developments in the Congress.

Sincerely,
David B. Allman, M.D., President
American Medical Association

May 6, 1958

Doctor F. J. L. Blasingame
General Manager
American Medical Association
535 North Dearborn Street
Chicago 10, Illinois

Dear Doctor Blasingame:

In discussing my bill on financing health care for the aged, I have repeatedly indicated my desire to receive constructive proposals and criticisms from the medical profession. I wish very much that a plan could be developed that would be satisfactory both to doctors and to the large numbers of people who want better methods of paying for medical care for our aged citizens.

In the hope of supplying aid in securing agreement, I want to present to the readers of The Journal of the American Medical Association a few facts and explanations which will counteract false impressions likely to arise from the A. M. A. leaflet, "Facts About the Forand Bill," and from Dr. Allman's letter of April 4 to A. M. A. members.

1. The proposal embodied in my bill deals with the financing of health care, not with the nature of that care. It would no more affect the relationships between doctors, hospitals and patients than does private insurance. Specific safeguards are included against government interference with methods of medical practice.

2. As to the extent of existing health insurance among the aged: a U. S. Public Health Service Survey shows that only 36.5% of the aged, (not 50% as stated) had some form of health insurance in September, 1956. Of those thus counted as "covered," however, a large proportion had health insurance that was inadequate in scope, amount, and dependability. The necessary costs of private insurance continue to keep adequate insurance beyond the reach of the majority of aged persons and accentuate the financial problems of physicians, hospitals and welfare agencies that have to care for them when ill.

3. Instead of "destroying" voluntary health insurance as the leaflet states, my proposal would relieve insurance companies, Blue Cross, Blue Shield and the hospitals of financial responsibility for a high-cost segment of the population.

4. Far from being "socialistic," H. R. 9467 would enable people to be assured of essential care through contributions they have themselves made, rather than reluctantly be compelled to seek direct government subsidy through relief programs on a means-test basis.

5. Doctors would continue to be responsible for determining when patients should be hospitalized, the nature of their care, and the length of their stay. Problems of unnecessary hospitalization and surgery already exist under private insurance and will continue to require whatever constructive action doctors and hospitals can develop. While the bill would increase the effective demand for care, the use of nursing homes would be encouraged by my bill as an alternative to hospitalization, at lower cost.

6. Careful cost estimates have been developed in the Department of Health, Education and Welfare based on U. S. experience, including also an analysis of the very different situation in Saskatchewan. Such estimates and other official statements readily available from the Social Security Administration will show that there is no reason for fears that my proposal would cost so much as to "jeopardize the retirement of millions of Americans."

7. The A. M. A. leaflet does not mention that my bill would also raise the monthly cash payments to beneficiaries of old-age, survivors and disability insurance. The higher tax rates which the leaflet quotes are planned to cover both the costs of this average 10% increase and also the health benefits.

Sincerely yours,
Aime J. Forand, M. C.

THE MEDICARE PROGRAM

April 25, 1958

The Honorable George H. Mahon, Chairman
Subcommittee on Department of
Defense Appropriations
House of Representatives
Washington, D. C.

Dear Mr. Mahon:

I am taking the liberty of writing you because of certain questions which I understand have been raised before your Subcommittee with respect to the "free choice" provision of the legislation enacted by Congress in 1956 authorizing medical care and hospitalization for dependents of service personnel.

The questions deal in part with the economy which would allegedly result by eliminating in some instances free choice by eligible dependents between private and service physicians and facilities. The American Medical Association does not agree that tax money would necessarily be saved if dependents of service personnel are denied a free choice. Furthermore, we are convinced that elimination of free choice would result in lessening the amount of authorized medical care now available to and received by the dependents.

It is difficult for many reasons to make an accurate cost comparison between civilian and military medical care and hospitalization. Depreciation

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Representative Aime J. Forand of the 1st District in Rhode Island is Chairman of the Subcommittee on Technical and Administrative Problems on Excise Taxes and is a member of the Ways and Means Committee, Democratic Steering Committee, and the Democratic Committee on Committees.

costs, fringe benefits, as well as the expenses involved in recruitment, training, etc., are not included in computing the cost of military medical care. In this connection, we would respectfully invite your attention to the statement of Dr. Hugh Hussey before the Senate Subcommittee on Defense Appropriations on June 19, 1957. In addition, any attempt at a comparison of costs must also take into consideration the types of cases involved. The Medicare program under Title II of P. L. 569, 84th Congress, has dealt predominantly with obstetrical cases which have a relatively high cost per hospital day.

The interchange in status between eligibility and non-eligibility for civilian care would most certainly compound administrative problems. This would make DD Forms 1173 meaningless with resulting confusion among not only the dependents but civilian physicians and hospitals as well.

Many of the costs to date in the administration of P. L. 569 have been of a non-recurring nature and were necessary in contracting for civilian care through the medical associations, hospitals and their designated fiscal agencies. A significant part of this cost was for informing all parties and agencies concerned. Any change at this time would only entail further disruption in administrative mechanisms and would result in the total loss of the non-recurring expenses of inaugurating the program.

To eliminate the free choice provision in the law, as spelled out in the "implementing directives," would necessitate in many instances the exclusive utilization of military and naval facilities staffed by physicians in the uniformed services. Should this occur, and should the armed services take over the civilian phase of Medicare, or a substantial part of it, an increased demand for physicians in uniform would also undoubtedly result—a demand which could probably be met only by reactivation of discriminatory draft legislation.

In any thorough consideration of the program, it should be emphasized that dependents of those in the uniformed services are civilians and should seek their medical treatment through civilian channels if we are to preserve the beneficial aspects of our present system of providing medical care and to guard against further maldistribution of professional health personnel.

The Medicare program has been accepted by dependents of service personnel and by the medical profession and it is our understanding that it has been successful. We have also been advised that it has been economically and wisely administered. It is, therefore, our sincere recommendation that no major change affecting choice between civilian and military facilities be made in the Medicare program at this time.

Sincerely,
F. J. L. Blasingame, M.D.
General Manager

COMMITTEES ON AGING

April 30, 1958

The Honorable Roy W. Wier, Chairman
Safety and Compensation Subcommittee
Committee on Education and Labor
House of Representatives
Washington, D. C.

Dear Mr. Wier:

I should like to take this opportunity to express the endorsement by the American Medical Association of H. R. 9822 and H. R. 11835, 85th Congress, bills to provide for holding a White House Conference on Aging and to assist states in conducting similar conferences on aging prior to the White House Conference.

The American Medical Association has had a deep and longstanding interest in the problems of our aged citizens, especially in regard to their health needs. Our Committee on Aging, established in 1955, is composed of some of the leading medical authorities in the country on the health problems of older persons. This Committee has recently conducted regional conferences on aging in Seattle, Dallas, Philadelphia, Birmingham, and Omaha. The American Medical Association has also scheduled a national conference on aging to be held in Chicago in September. Up to the present time, approximately thirty State Medical Societies have created Committees on Aging and by September it is expected that approximately forty such Committees will have been formed.

In addition to the activities of its Committee on Aging, the American Medical Association has recently joined with the American Dental Association, the American Hospital Association and the American Nursing Home Association in establishing a Joint Council to Improve the Health Care of the Aged. Although studies of the problems of the aged have been under way for the past several years by these various organizations, research in this field will now be intensified through joint efforts, and projects for meeting the problem will be activated as rapidly as possible.

The American Medical Association believes very strongly that there is a need for systematic interchange of ideas in this field. Through our experience with our regional conferences on aging and through our activities as a member of the Joint Council, we have learned that much is to be gained from state and national conferences on this subject, such as proposed in H. R. 9822 and H. R. 11835. The members of the medical profession will take part in these conferences, both on the state and national levels, to the fullest extent possible.

We are aware that the Committee is studying a number of bills which would establish a Bureau of Older Persons in the Department of Health, Education, and Welfare or a U. S. Commission on

Aging. The American Medical Association recommends that action on these bills be deferred until after the White House Conference on Aging. It may be anticipated that the Conference will include these bills in its deliberations.

I would request that this letter be made a part of the record of the hearings of your Committee and if your Committee desires any further information from our Association or the personal appearance of a representative, we would be most happy to comply.

Sincerely yours,
F. J. L. Blasingame, M.D.
General Manager

FEDERAL MEDICAL LEGISLATION[1]

85th Congress

Social Security

An increasing number of bills relative to changes in Social Security are being dropped into the congressional hopper. Since many of the bills are similar or identical to previous bills, they will only be listed by number and author. References to similar bills which have been discussed previously will be given.

H. R. 10844 by Congressman Moore and H. R. 10869 by Congressman Neal (Republicans, W. Va.) are similar to S. 1811 by Senator Revercomb (R., W. Va.) and would provide a more liberal definition of "disability" for the purpose of receiving disability insurance benefits. Under this bill an individual who could not obtain employment because of his disability would be eligible for disability benefits.

H. R. 10845 and H. R. 10868 by Congressmen Moore and Neal, respectively, are similar to S. 1812 by Senator Revercomb (R., W. Va.) and apply to disability benefits and liberalization of the requirements, making an applicant eligible for benefits if he has "at least one quarter (3 months) of coverage."

H. R. 10974 by Congressman Dent, H. R. 10975 by Congressman Holland (Democrats, Pa.), and H. R. 10977 by Congressman Libonati (D., Ill.) are identical bills which would amend the Social Security Act to provide, among other things, increased benefits, and would increase the wage base and rate of tax. Retirement age would be reduced to age 60 for both men and women. The amendments would also eliminate age requirements for spouse benefits when the wage earner became eligible. Widows and widowers would also become entitled to benefits upon the death of the wage earner. Benefits would be increased, with the minimum benefit being $50 per month. Maximum family benefits would be increased from the present $200 to $250. The maximum income a recipient would be allowed to earn before suffering a reduction of benefits would be reduced from the present level of $1,200 to $600 annually. To pay for the increased benefits the base wage scale would be increased from the present rate of $4,200 to $5,000. In addition, the tax rate for both employee and employer would be increased by 0.5% for each, and by 0.75% for self-employed in 1959, 1960, and every 5 years thereafter until 1975. By 1975 self-employed with an income of over $5,000 would be paying $356.25 annually and the employed individual and his employer would each be paying $237.50 for social security coverage.

H. R. 11095 by Congressman Holtzman (D. N. Y.) is identical to H. R. 11396 by Congressman Dollinger (D., N. Y.), and both are similar to S. 173 by Senator Langer (R., N. D). These bills would eliminate the age 50 requirement for disability benefits, reduce the retirement age of men to 60 and for women to 55, and remove the limit of $1,200 that an individual could earn before benefits are reduced.

H. R. 11164 by Congressman Fino (R., N. Y.) is similar to H. R. 7834 by Congressman Shelley (D., Calif.) and would allow disability benefits for a survivor widow after age 50 if she becomes disabled.

S. 3419 by Senator Thye (R., Minn.) would eliminate the present requirement under the disability freeze and the disability benefits provisions of the Social Security Act, which requires that an individual must be covered for 5 out of the 10 years preceding the disability. An individual would still be required to be currently covered (coverage for 1½ years out of the 3 years preceding the onset of the disability) and also be fully insured (40 quarters of coverage or coverage for one-half the quarters since 1950, with a minimum of six quarters).

H. R. 11331 by Congressman Porter (D., Ore); H. R. 10664 by Congressman Ashley (D., Ohio); H. R. 10532 by Congressman Dellay (D., N. J.); and H. R. 9467 by Congressman Forand (D., R. I.) are all identical and have been previously discussed under the "Forand Bill." (The number of labor-dominated congressmen climbing on the band wagon continues to grow.)

H. R. 10730 introduced by Congressman Sheppard (D., Calif.) is similar to H. R. 5129 by Congressman King, H. R. 5278 by Congressman Roosevelt, H. R. 10820 by Congressman Doyle, and H. R. 10962 by Congressman Saund (Democrats, Calif.) and would provide for increased payments by the federal government to the states for carrying out the public assistance programs (aid to aged, dependent children, the blind, and the permanently and totally disabled). The government would contribute one-half of cost to the state for administration of the program and "one-half of the totals of sums expended . . . in the form of medical or any other type of remedial care. . . ." The bill would also remove the ceiling of the $60 maximum monthly payments now contained in the law. It would also require a state to participate in all four categorical programs in order to be eligible for payment under any one of the programs. It would enable

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[1] From the Washington Office of the American Medical Association.

Billings Hospital, when Karl P. Link, Ph.D., professor of bacteriology, University of Wisconsin, Madison, will speak on "Anticoagulants—Where Are We Now?"

Visiting Professor at La Rabida.—Howard J. Rogers, Ph.D., of the Medical Research Council at the National Institute for Medical Research, Mill Hill, London, England, is visiting professor at the La Rabida–University of Chicago Institute for the quarter ending June 14. Dr. Rogers is deputy chairman of the editorial board of the *Biochemical Journal.*

Contributions for Cancer Research.—The Nathan Goldblatt Research Fund has presented to the University of Chicago $100,000, the first payment on a new pledge of $250,000 which will contribute to expansion of the university's cancer research facilities. In addition, the Nathan Goldblatt Society for Cancer Research has pledged $100,000 toward the cost of the new unit of the University Clinics. The new building, two stories and a basement, will connect the Chicago Lying-in Hospital with Bobs Roberts Memorial Hospital for Children. By permitting relocation of outpatient service, it will provide space for expansion of research in cancer and other diseases in Billings Hospital of the clinics. Since 1948, following a gift of one million dollars from the Goldblatt Brothers Foundation in 1947 for the Nathan Goldblatt Memorial Hospital, Goldblatt Brothers Employees Organization grants toward cancer research at the university have totaled $419,000, and the Nathan Goldblatt Society support is about $440,000.

INDIANA

Summer Camp for Diabetic Children.—The Indianapolis Diabetes Association will sponsor the James Whitcomb Riley camp for diabetic children for the fourth consecutive year. The camp session will open Aug. 3 and conclude Aug. 22. The facilities of the Riley Memorial Association and Indiana University will be used. The camp is in the Brandford Woods Outdoor Education area six miles north of Martinsville near State Highway 67. Diabetic children from 8 through 16 years of age are eligible. The program will be conducted on a nonsectarian basis without restrictions as to race or creed. Campers will be under constant medical and nursing care; qualified dietitians will supervise meals; and a laboratory will be operated for all necessary tests incident to the control of diabetes. Applications will be received only for the full session. The fee for the three weeks is $150, which includes all diabetic supplies and necessary laboratory procedures. Funds are available for financial assistance to children whose families are unable to pay the full amount. Information may be obtained from the Indianapolis Diabetes Association, Inc., 821 Hume Mansur Building, Indianapolis 4, Ind.

MASSACHUSETTS

Award Cancer Grant to Dr. Wotiz.—Herbert H. Wotiz, Ph.D., associate director, hormone research laboratory, Boston University School of Medicine, has been awarded a $115,000 grant by the U. S. Public Health Service for a four-year study on the functions of hormones in relation to cancer. The research is part of a continued study by Dr. Wotiz and the school laboratory. Dr. Wotiz and three associates were awarded first prize in the section of experimental medicine and therapeutics at the A. M. A. meeting in New York last summer for an exhibit of "Estrogen Biosynthesis by Post-Menopausal Human Ovaries."

Personal.—Dr. Robert S. Schwab has been elected chairman of the Medical Advisory Board of the Myasthenia Gravis Foundation. Dr. Schwab, neurologist at the Massachusetts General Hospital since 1937, has served on the executive committee of the foundation's medical board since its inception in 1952.——Dr. Helmuth Ulrich, of Newton, has received the "Man of the Year" award of the Boston University Medical School Alumni Association. Dr. Ulrich, who graduated in 1911, is the fifth alumnus to receive the citation.——Dr. Merrill C. Sosman, emeritus professor of roentgenology, Harvard Medical School and emeritus roentgenologist-in-chief of the Peter Bent Brigham Hospital, Boston, gave the fourth annual W. J. and C. H. Mayo Memorial Lecture on "The Accuracy of X-Ray Diagnosis" at Carpenter Hall, Dartmouth College, Hanover, N. H., March 29.

NEW JERSEY

Establish Kump Memorial Grant.—The board of trustees of the Medical Society of New Jersey has authorized the establishment of the Albert Barker Kump Memorial Grant in the Medical Student Loan Fund of the society. The goal is $5,000. Dr. Kump, who was president of the society, died April 18. Contributions (payable to the society) and requests for information should be sent to The Albert Barker Kump Memorial Grant, the Student Loan Fund of the Medical Society of New Jersey, P. O. Box 904, Trenton 5, N. J.

Personal.—Governor Robert B. Meyner has announced the appointment as of March 14 of Dr. Luke A. Mulligan to the State Board of Medical Examiners for a term of three years.——Dr. Charles Hendee Smith has become a member of the Princeton Medical Group. He will continue to see patients in consultation in the New Brunswick Pediatric Group in which he has practiced for the last 16 years. Dr. Smith is 81.—The Secretary of the British Medical Association invited Dr. Edward M. Miller, of Englewood, to deliver the Annual British Medical Association Lecture to the North Middlesex Division of the B. M. A. on March 31. His subject was "Surgical Management of Carcinoma of the Colon."

New Medical Center in Livingston.—Ground-breaking ceremonies for a 10-million-dollar "hospital of tomorrow" were held May 3 in Livingston. Trustees of Saint Barnabas Medical Center, Newark, said that patients in the new center will be grouped according to the intensity of illness, made possible by three separate patient areas: (1) an admission area where patients will be admitted to a private or semiprivate room on the ground floor to remain until tests are completed and diagnosis is determined; (2) An intensive care area where all surgical patients will go for special care immediately after leaving the recovery room; (3) A convalescent area on an upper floor for patients no longer needing intensive care. On the ground floor will be the admission area, intensive care area, and operating, cystoscopic, and fracture rooms, recovery room, clinical and x-ray laboratories, outpatient and rehabilitation departments. According to the trustees, this will enable one-third more patients to be treated without increasing the number of personnel. The new center, located on 60 acres overlooking the Kittatiny mountain range, will be a nondenominational, nonprofit general hospital with 400 beds and 75 bassinets. The project will be completed in 1959-1960.

NEW YORK

Inaugurate President at Upstate Medical Center.—Carlyle F. Jacobsen, Ph.D., will be inaugurated as first president of the State University of New York Upstate Medical Center in Syracuse at commencement exercises June 8, 2:30 p. m., in Nottingham Auditorium. Welcoming Dr. Jacobsen to office on behalf of the faculty will be Wilfred W. Westerfeld, Ph. D., chairman, department of biochemistry, and formerly acting dean of the Center. Dr. Jacobsen assumed the post of president of the center and dean of its College of Medicine on Dec. 1, 1957. He was previously executive dean for medical education of the State University of New York.

Personal.—The University of Buffalo School of Medicine and Buffalo General Hospital honored Dr. Thomas F. Frawley, head, sub-department of endocrinology and metabolic diseases, Albany Medical College, when they chose him as their first visiting professor for a week, April 14-20.—Dr. Victor N. Tompkins has been appointed assistant commissioner of health for the State Health Department's Division of Laboratories and Research, effective April 1, succeeding Dr. Gilbert J. Dalldorf, who left to become associate medical director of the National Foundation for Infantile Paralysis in January.—Bernard Saper, Ph.D., has been appointed director of psychological services in the New York State Department of Mental Hygiene, succeeding Elaine F. Kinder, Ph.D. He will assume his duties July 1.—Franklyn N. Arnhoff, Ph.D., clinical assistant professor of psychiatry, Syracuse University College of Medicine, has been granted a faculty fellowship in social gerontology by the Inter-University Council on Social Gerontology of the University of Michigan, Ann Arbor, for advanced study in gerontology for the month of August at the University of Connecticut, New Haven.

New York City

Dr. Dubos Wins Ricketts Award.—Rene J. Dubos, Ph.D., bacteriologist, Rockefeller Institute for Medical Research, received the Howard Taylor Ricketts award for 1958 recently at the University of Chicago when he lectured on "Nutrition, Emotion and Infection." The prize, consisted of a medal and a cash stipend of $200. Born and educated in France, Dr. Dubos came to the United States in 1924, and he has been associated continuously with the Rockefeller Institute of Medical Research since 1927 except for two years when he was George Fabyan professor of comparative pathology and tropical medicine at Harvard Medical School, Boston. The Howard Taylor Ricketts award was established by Mrs. Howard T. Ricketts in memory her husband who died May 3, 1910, in Mexico City while doing research on typhus fever. He was a prominent faculty member of Rush Medical College.

NORTH CAROLINA

Courses in Air Pollution.—The University of North Carolina's Department of Sanitary Engineering in the School of Public Health, Chapel Hill, has announced courses in air hygiene and air pollution control made possible under a grant from the U. S. Public Health Service. The first of these courses has been initiated, with expansion to three during the 1958-1959 school year. The plan provides a concentration in air pollution control based on the principles of air hygiene, which may concurrently fill the prerequisites for courses in industrial hygiene. Inquiries should be addressed to Prof. Daniel A. Okun, Box 899, Chapel Hill, N. C.

Open Another Poison Control Center.—The second Poison Control Center in the State opened at Onslow Memorial Hospital in Jacksonville May 1. Dr. Samuel C. Cox is director of the center and Dr. Eleanor H. Williams, Onslow County Health Director, is assistant director. The telephone numbers are 7241 & 7242. The center will be able to provide information as to ingredients, toxicity, symptoms, and preferred treatment of many of the potentially poisoning trade-name products. The Onslow Poison

Control Center is making its services available specifically to all physicians in the Third District of the State Medical Society and to any others who may wish to use it.

Students Win Pathology Awards.—Two fourth-year medical students of the University of North Carolina School of Medicine, Chapel Hill, have won awards in nation-wide competition for papers presented on research they did in the field of inheritance of human diseases. They are W. R. Bullock Jr., of Bethel, and Vernon McFalls, of Greensboro. Both received Sheard-Sanford prizes which are presented annually by the American Society of Clinical Pathologists in the form of cash grants. Their work was done under the supervision of Dr. John B. Graham, associate professor of pathology at the Medical School. Bullock's paper was on "Carrier State of Plasma Thromboplastin Component Deficiency," while McFalls' paper dealt with "Genetic Study of Vitamin D. Resistant Rickets and Hypophosphatemia."

PENNSYLVANIA

Philadelphia

Students Win Research Awards.—Five University of Pennsylvania medical students received special prizes and awards at the Medical School's 50th annual Undergraduate Medical Association Day, April 24. The awards are annual honors to medical students doing "the best medical research" in various fields of interest:

The annual Borden Undergraduate Research Award in Medicine ($500) awarded to Stanley M. Boulas, of Providence, R. I., is presented to that member of the fourth-year class "whose research has been determined to be the most meritorious performed by all similarly eligible persons."

The Mary Ellis Bell Prize, presented to Robert Byck, a junior medical student from Newark, N. J., was presented "for outstanding medical research."

The Rose Meadow Levinson Memorial Prize was awarded to William H. Hardesty, senior medical student from Northfield, Minn., for his presentation of the "best paper dealing with cancer."

Theodore R. Bledsoe, junior medical student from Silver Spring, Md., won the John G. Clark prize "for the best paper dealing with obstetrics and gynecology."

The O. H. Perry Pepper Prize, given to Gordon B. Avery, of Washington, D. C., is presented to the medical senior "who has performed investigative work of exceptional merit during his four years, and who has also demonstrated noteworthy competence as a clinician."

WISCONSIN

Institute on Alcohol Studies.—The third annual meeting on alcohol problems, sponsored jointly by the University of Wisconsin Extension Division, Western Michigan University, the Wisconsin Council on Alcoholism, and the Michigan State Board of Alcoholism, will be held June 23-27. Keynote speaker, Selden D. Bacon, Ph.D., professor of sociology, Yale University, New Haven, Conn., will open the institute with a discussion on "Problems of Alcohol Orientation." Discussion topics include: physiological, social, economic, educational, and legal aspects of the alcohol problem. A special feature will be a teenage panel discussing problems of teenage drinking. Information may be obtained from Prof. John L. Miller, Ph.D., director, 1958 Midwest Institute on Alcohol Studies, 206 Extension Building, Madison 6, Wis.

GENERAL

Fellowships in Psychiatry.—The American Psychiatric Association has announced the award of 10 Smith Kline & French Foundation fellowships in psychiatry totaling $13,150, which are the final awards of the three-year $90,000 grant established in 1955 to provide a broad range of training opportunities in psychiatry. The foundation recently awarded a $100,000 grant to the American Psychiatric Association to continue the fellowships through 1960. A total of 14 recipients, including 10 medical students, will benefit in the latest group of grants. The fellowships are administered by a committee named by the association, with Dr. Kenneth E. Appel, Philadelphia, as chairman.

International Prize for Medical Ethics.—The "John XXI" International Prize for Medical Ethics, instituted at the Paris Congress in 1951 by the Association of Portuguese Catholic Doctors, has been announced by the International Secretariate of Catholic Doctors. The competition theme will be "Responsibility of the Doctor Before the Actual World" and the following rules apply:

(1) The prize will consist of a bronze medal and a sum of 5000 Belgian franks or the equivalent.
(2) The prize will be awarded at the Eighth International Congress of Medical Doctors to the best work on medical ethics concerning the theme of the competition. The work must be supplied with a typed translation in English or French in seven copies. The work must include 20 to 30 pages with about 25 lines on a page.
(3) The competitors should send their work to the International Secretary, 5, rue Guimard, Brussel, before July 1, together with an application for admission.

Medical Education Tour of South America.—Dr. Carl F. Schmidt, chairman, department of pharmacology, University of Pennsylvania, is one of three medical scientists appointed by the International Union of Physiological Sciences to visit South America to discuss problems of medical education and research. Dr. Schmidt left May 14 to join Drs. C. Heymans, professor of pharmacology, University of Ghent, Belgium, and Ragnor A. Granit, professor of physiology, Karolinska Institute, Stockholm, Sweden, for a six-week tour of South American medical education and research facilities. The three-man team of the International Union, an affiliate of the World Health Organization, will visit medical schools and facilities in Venezuela, Brazil, Uruguay, Argentina, Chile, Peru, Colombia, Panama, and Mexico. During the tour, Dr. Schmidt will appear at the various medical schools as a guest lecturer. A member of the National Academy of Sciences and a past-president of the American Society for Pharmacology Dr. Schmidt is also editor-in-chief of *Circulation Research*.

Meeting of Medical Women in San Francisco.—The annual meeting of the American Medical Women's Association, will be held June 19-22, with headquarters at the Sir Francis Drake Hotel, San Francisco. The Woolley Memorial Lecture will be presented June 20, 7 p. m., by Dr. Jessie M. Bierman, of the University of California School of Health, San Francisco. Following presentation of the Elizabeth Blackwell award by Dr. Alma D. Morani, Dr. Katharine W. Wright, president of the Association, will present an inauguration address, "Group Participation—Keynote of the Future." A luncheon panel on "The Physician in the Role of Advisor," moderated by Dr. Rosa Lee Nemir, will include the following subtopics and participants:

In the Home, Dr. Judity E. Ahlem, Livermore, Calif.
In High School, Dr. Mary A. M. Henry, San Antonio, Texas.
In College, Dr. Mary S. K. Helz, State College, Pa.
In the Community, Dr. Jessie Laird Brodie, Portland, Ore.
In the Physician's Office, Dr. Camilla M. Anderson, Salt Lake City, Utah.

A program of entertainment is arranged. For information write the American Medical Women's Association, Inc., 1790 Broadway, Room 315, New York 19.

Announce Six Ophthalmology Fellowships.—Six fellowships for residents in ophthalmology, to begin July 1, have been announced by the Guild of Prescription Opticians of America, Inc. Applications for these fellowships must be received by June 13. Each fellowship is for a total of $1,800, payable in monthly stipends over the period of a three-year residency. The grants are limited to residencies at approved institutions where full three-year residencies are offered. Each grant is made for the entire three years, to begin the first year. Application forms are available by writing Fellowships, Guild of Prescription Opticians of America, Inc., 110 E. 23rd St., New York 10. The new fellowships represent one for each of six areas into which the U. S. and Canada have been divided on the basis of a nearly equal number of eligible residencies in each area. The selection of the resident fellow is made by a committee of ophthalmologists in each area. The guild provides all fellowship funds as well as the program's cost of administration. Together with the 6 guild fellowships awarded in 1956 and the 5 last year, this year's new fellowships will bring the total to 17.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	May 10, 1958		May 11, 1957
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	1
Massachusetts	..	..	1
Rhode Island	..	..	..
Connecticut	..	..	1
Middle Atlantic States			
New York	..	..	1
New Jersey	..	1	..
Pennsylvania	..	..	2
East North Central States			
Ohio	..	..	1
Indiana	..	..	..
Illinois	..	..	..
Michigan	..	..	..
Wisconsin	..	..	1
West North Central States			
Minnesota	..	..	1
Iowa	..	..	..
Missouri	..	..	2
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	..	..	1
Kansas	..	..	1
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	..	..	1
West Virginia	..	..	..
North Carolina	..	..	..
South Carolina	..	..	..
Georgia	..	..	..
Florida	..	..	5
East South Central States			
Kentucky	..	..	1
Tennessee	..	1	..
Alabama	..	..	..
Mississippi	..	3	2
West South Central States			
Arkansas	..	..	1
Louisiana	..	..	8
Oklahoma	..	..	..
Texas	4	5	15
Mountain States			
Montana	..	..	..
Idaho	..	..	1
Wyoming	..	..	3
Colorado	..	1	..
New Mexico	..	..	2
Arizona	1	3	1
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	..	..
Oregon	..	..	..
California	2	5	18
Territories and Possessions			
Alaska	..	..	..
Hawaii	..	..	..
Puerto Rico	3	3	..
Total	10	22	71

Meeting on Goiter in San Francisco.—The 1958 annual meeting of the American Goiter Association will be held in the St. Francis Hotel, San Francisco, June 16-19. On June 16 operative clinics, and a panel discussion, "Carcinoma of the Thyroid Gland," will be held at Moffitt Hospital. Forty-four papers are scheduled for the five sessions, including the following by foreign authors:

Functional Relation Between the Liver, the Thyroxine-Binding Protein, and the Thyroid, Dr. Alfred Vannotti, Lausanne, Switzerland.
Studies on the Effect of TSH on Human Thyroid Function, Drs. Jerzy Einhorn and Lars Gunnar Larsson, Stockholm, Sweden.
Hypothalamic-Adrenal-Thyroid Relationships, Dr. Geoffrey W. Harris, London, England.

Dr. Elmer C. Bartels, Boston, will present the presidential address the afternoon of June 18. A ladies' program is arranged. For information write the American Goiter Association, Dr. John C. McClintock, Secretary, 149½ Washington Ave., Albany, N. Y.

Endocrine Society Meeting in San Francisco.—The 40th annual meeting of the Endocrine Society will be held in the St. Francis Hotel, San Francisco, June 19-21. Over 80 papers are scheduled for presentation at seven sessions under the following headings: endocrine and metabolic interrelationships, thyroid and parathyroids, adrenal and gonads, pituitary and hypothalamus, gonads and reproduction, diabetes and metabolism, and adrenal. The eighth session will be devoted to clinical panels with the following chairmen:

Endocrine Treatment of Neoplastic Disease, Dr. Olof H. Pearson, New York City.
Hyperparathyroidism and Bone Disease, Dr. Gilbert S. Gordon, San Francisco.
Chemical Treatment of Diabetes, Dr. Peter H. Forsham, San Francisco.
Intersexuality, Dr. Warren J. Nelson, Safford, Ariz.

Leo T. Samuels, Ph.D., will present the presidential address at the annual dinner, June 20, 7:30 p. m. For information write Dr. Henry H. Turner, 1200 N. Walker St., Oklahoma City 3, Okla., secretary of the society.

Fellowship in Heart Research.—The American Heart Association has announced the award of $1,433,147 to 183 scientists for research on heart and blood vessel diseases. Continued emphasis will be given in these studies to basic research in factors underlying disorders of the heart and circulation. Support will also be given for investigators working on a wide range of problems affecting the welfare and treatment of heart patients. The awards go into effect on July 1. Dr. Robert W. Wilkins, president of the association, pointed out that all these awards were made possible by voluntary public contributions to the annual Heart Fund appeal and they represent the first part of the 1958-1959 national research support program. A second group of national awards, in the grant-in-aid category, will be announced within the next few months. The 183 scientists named will pursue their studies in 29 states, the District of Columbia, England, and Denmark. Eighty-four of the awards are to "established investigators" (this category provides five years of uninterrupted support to mature scientists conducting independent research). Sixty-two of the awards are to research fellows; thirty-four to advanced research fellows. Given usually for two years, both of these fellowships enable young scientists to obtain training in research methods under experienced guidance. In addition, $59,000 was appropriated in departmental grants to help meet overhead costs incurred on behalf of established investigators.

Awards for Student Exhibits.—The first Student American Medical Association–Lakeside Laboratories awards, presented for "outstanding medical exhibits," were given to three exhibits at the Student A. M. A. meeting in Chicago recently. Top awards of $500 each plus the privilege of exhibiting their work at the American Medical Association convention in San Francisco, including a free trip to and week in that city, went to (1) Quinton Callies, junior of the University of Wisconsin School of Medicine, Madison, for his exhibit on work with Drs. Helen A. Dickie and John I. Rankin on "Farmer's Lung"; (2) Dr. Edward R. Duffie, intern at the Raymond Blank Memorial Hospital in Des Moines, Iowa, for an exhibit of work in endocardial fibroelastosis. The second and third student awards of $350 and $250, respectively, went to (1) Michael P. Kaye and Robert A. McDonald, of the Stritch School of Medicine of Loyola University, Chicago, for "Cardiac Augmentation," and (2) Olga Jonasson and Robert P. Hodam, of the University of Illinois Medical School, Chicago, for "The Viability of Cancer Cells in the Circulating Blood of Animals."

Conference on Cell Organization.—A conference on "The Chemical Organization of Cells, Normal and Abnormal" will be held in Madison, Wis., Aug. 21-23, supported by the National Institutes of Health as part of the program for increase in pathology research potential. Speakers include George O. Gey, Paul A. Weiss, Ph.D., Van R. Potter, Ph.D., Charles D. Kochakian, Ph.D., Albert J. Dalton, Ph.D., Dr. Sheldon C. Sommers, Choh H. Li, Ph.D., G. H. Bourne, Dr. Frederik B. Bang, David E. Green, Ph.D., Alfred G. Marshak, Ph.D., Dr. Henry Quastler. Interested persons should write Dr. Joseph J. Lalich, professor of pathology, University of Wisconsin, 426 N. Charter St., Madison, Wis. The National Institutes of Health has made funds available for a limited number of stipends to assist workers in basic science fields in attending the Madison conference. This money will be available after the first of July and will include the fees for the conference and up to a maximum of $200 for transportation. These funds are intended to support the travel and attendance of younger workers (a) in junior academic or research positions and (b) not already in recipt of research grants carrying stipends. Application should be made in writing to Dr. Joseph F. A. McManus, Chairman, Department of Pathology, University of Alabama Medical Center, Birmingham, Ala. A letter from the chairman of the department should accompany each plication. Requests for accommodation should made to Dr. Lalich at the same time.

Meeting on Electroencephalography in Atlantic City.—The 12th annual meeting of the American Electroencephalographic Society will be held June 12-15 at the Hotel Traymore, Atlantic City, N. J. Dr. Robert S. Dow will give the presidential address the morning of June 14 and will serve as chairman for a symposium on "Electrophysiology of the Cerebellum," which will include the following topics and participants:

Introduction and Historical Survey, Dr. Dow.
Cerebellar Responses to the Stimulation of Afferent Connections, Dr. Ferdinando A. Morin, Detroit.
Electrical Activity of the Cerebellar Cortex and Nuclei and How It May Be Modified, John M. Brookhart, Ph.D., Portland, Ore.
Efferent Discharges Resulting from Electrical Stimulation of the Cerebellar Cortex and Nuclei, Ray S. Snider, Ph.D., Chicago.
Significance of Electrophysiological Studies in Relation to the Localization of Function in the Cerebellum, Dr. William W. Chambers and James M. Sprague, Ph.D., Philadelphia.
Relation of the Cerebellum to Sensory Mechanisms, Dr. Dow.

Twenty-five papers are scheduled and a symposium on EEG of the "Premature, Newborn and Young Infant" is planned for June 15. Speaker at the annual banquet (June 14, 7 p. m.) will be Donald B. Lindsley, Ph.D., who will discuss "Lindsley's Folly: Reminiscences About the Early Days of EEG During the Depression Era (1930-1940)." For information write Dr. Jerome K. Merlis, Secretary, American Electroencephalographic Society, EEG Laboratory, University Hospital, Baltimore 1, Md.

FOREIGN

International Meeting of Gynecologists and Obstetricians.—The International Professional Association of Gynecologists and Obstetricians will meet in Brussels, Belgium, under the presidency of Dr. Francisco Luque Beltrán, of Madrid, July 18-19. Two main subjects to be discussed are: "Criteria and Processes of Specialization in Gynecology and Obstetrics" and "Economic Classification of Fees for Obstetric and Gynecologic Functions According to the Hierarchy of Values." Registration fee is 500 Belgian francs to be deposited to the account of l'Association Professionnelle des Obstetriciens et Gynecologues Belges: Dr. Stocq, 23 Drève du Caporal Uucle, Banque de la Société Générale de Belgique, Brussels, Belgium. Information can be requested from the General Secretary of the Congress, Dr. Geeraert, 211, Avenue Louise, Brussels, Belgium.

DEATHS IN OTHER COUNTRIES

Tobias Levitt.—Formerly surgical first assistant at the thyroid clinic, New End Hospital, Hampstead, England, Tobias Levitt, F. R. C. S., died in Charing Cross Hospital Feb. 22. He was elected to give a Hunterian Lecture at the Royal College of Surgeons (1952), was author of "The Thyroid: A Physiological, Pathological, Clinical, and Surgical Study," and was attached to the Royal Marsden Hospital in a research capacity (since 1956). He was awarded a travelling fellowship by the Kellogg Foundation and by the International College of Surgeons, spending a year in the U. S. lecturing on diseases of the thyroid.

CORRECTIONS

Occupational Cancer.—In the report to the Council on Industrial Health in the April 26, 1958, issue of The Journal, Page 2177, column 1, second new paragraph, the equation starting on line 3 should read as follows: "Incidence (cases per 100,000 per year) $= [\text{total number of cases for } n \text{ years} \div (\text{population at risk} \times n)] \times 100{,}000$." The equation starting on the fifth line from the end of the same paragraph should read: "Incidence $= [10 \div (100 \times 10)] \times 100{,}000 = 1{,}000$ per 100,000 per year."

Aero Medical Association.—In the Washington News in The Journal, Feb. 22, 1958 issue, front advertising page 27, and April 5, 1958 issue, front advertising page 27, it was stated that the Aero Medical Association was "now nine years old" and was "formed ten years ago," respectively. These statements were erroneous. The Aero Medical Association was founded in 1929. The 30th anniversary will be observed at the association's annual meeting in Los Angeles, April 27-29, 1959.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: The American medical qualification examination to be given henceforth twice a year for foreign medical graduates. Medical Schools in the United States and Foreign Countries, Sept. 23. Final date for filing application is June 23. Executive Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Illinois.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: *Written. Parts I and II.* All medical centers in the United States and Canada, June 17-18. Sec., Dr. John P. Hubbard, 133 S. 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination.* Montgomery, June 17-19. Sec., Dr. D. G. Gill, State Office Building, Montgomery 4.

Arizona:* *Examination.* Phoenix, July 16-18. *Reciprocity.* Phoenix, July 19. Sec., Dr. Thomas N. Bate, 826 Security Bldg., Phoenix.

California: *Written Examination.* San Francisco, June 16-19; Los Angeles, August 18-21; Sacramento, Oct. 20-23. *Oral Examination.* San Francisco, June 14; Los Angeles, August 16; San Francisco, November 15. *Oral and Clinical Examination for Foreign Medical School Graduates.* San Francisco, June 15; Los Angeles, August 17; San Francisco, November 16. Sec., Dr. Louis E. Jones, 1020 N Street, Sacramento.

Colorado:* *Examination and Reciprocity.* Denver, June 10-11. Exec. Sec., Mrs. Beulah H. Hudgens, 715 Republic Bldg., Denver 2.

Connecticut:* *Examination.* Hartford, July 8-10. Sec., Dr. Creighton Barker, 160 St. Ronan St., New Haven.

Delaware: *Examination and Reciprocity.* Dover, July 8-10. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

Florida:* *Examination.* Miami, June 29-July 1. Sec., Dr. Homer L. Pearson, 901 N. W. 17th St., Miami.

Georgia: *Examination.* Atlanta and Augusta, June 11-12. *Reciprocity.* Atlanta, June 13. Sec., Mr. C. L. Clifton, 224 State Capitol Bldg., Atlanta.

Idaho: *Examination.* Boise, July 14-16. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Illinois: *Written Examination.* Chicago, July 7-11. *Oral Reciprocity Examination.* Chicago, July 11. Supt. of Regis., Mr. Frederic Selcke, Capitol Bldg., Springfield.

Indiana: *Examination.* Indianapolis, June 18-20. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Iowa:* *Examination.* Iowa City, June 16-18. Exec. Sec., Mr. Ronald V. Saf, State Office Bldg., Des Moines 19.

Kansas:* *Examination.* Kansas City, June 13-14. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Kentucky: *Written Examination.* Louisville, June 9-11. Sec., Dr. Russell E. Teague, State Board of Health, Louisville 2.

Maine: *Examination.* Augusta, July 8-10. *Reciprocity.* Augusta, July 8. Sec., Dr. Adam P. Leighton, 142 High St., Portland.

Maryland: *Examination.* Baltimore, June 17-20. Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

Massachusetts: *Examination.* Boston, July 15-18. Sec., Dr. Robert C. Cochrane, Room 37 State House, Boston.

Michigan:* *Examination.* Ann Arbor and Detroit, June 9-11. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

Minnesota:* *Examination.* Minneapolis, June 17-19. *Reciprocity.* Minneapolis, June 19. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

Mississippi: *Examination.* Jackson, June 23-24. *Reciprocity.* Jackson, June 25. Asst. Sec., Dr. R. N. Whitfield, Old Capitol Bldg., Jackson 113.

Montana: *Examination and Reciprocity.* Helena, Oct. 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination.* Omaha, June 16-18. Sec., Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

New Hampshire: *Examination.* Concord, Sept. 10-13. *Reciprocity.* Concord, Sept. 10. Sec., Dr. Mary M. Atchison, Room 101, 61 South Spring St., Concord.

New Jersey: *Examination.* Trenton, June 17-20. Sec., Dr. Patrick H. Corrigan, 28 W. State St., Trenton.

New York: *Examination.* Albany, Buffalo, New York City and Syracuse, June 24-26. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

North Carolina: *Examination.* Raleigh, June 16-19. *Reciprocity.* Raleigh, June 17 and Blowing Rock, July 25. Asst. Sec., Mrs. Louise J. McNeill, Professional Bldg., Raleigh.

North Dakota: *Examination.* Grand Forks, July 9-11. *Reciprocity.* Grand Forks, July 12. Sec., Dr. C. J. Glaspel, Grafton.

Ohio: *Examination.* June 19-21, Sec., Dr. H. M. Platter, 21 West Broad St., Columbus 15.

Oregon:* *Examination.* Portland, July 16-17. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

Pennsylvania: *Examination.* Philadelphia and Pittsburgh, July 8-10. Acting Sec., Mrs. Marguerite G. Steiner, Box 911, Harrisburg.

Rhode Island:* *Examination.* Providence, June 26-27. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

South Carolina: *Examination.* Columbia, June 24-25. Sec., Dr. H. E. Jervey, 1329 Blanding St., Columbia.

South Dakota:* *Examination.* Rapid City, August 12-13. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Tennessee:* *Examination.* Memphis, Madison and Dunlap, June 11-12; Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

Texas:* *Examination and Reciprocity.* Fort Worth, June 23-25. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Utah: *Examination.* Salt Lake City, July 9-11. Director, Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

Vermont: *Examination.* Burlington, June 19-21. *Reciprocity.* Burlington, June 19. Sec., Dr. F. J. Lawliss, Richford.

Virginia: *Examination.* Richmond, June 12-14. *Reciprocity.* Richmond, June 11. Address: Board of Medical Examiners, 631 First St., S. W., Roanoke.

Washington:* *Examination.* Seattle, July 14-16. Administrator, Mr. Thomas A. Carter, Capitol Bldg., Olympia.

West Virginia: *Examination and Reciprocity.* Charleston, July 14-16. Sec., Dr. N. H. Dyer, State Office Bldg., No. 5, Charleston.

Wisconsin:* *Examination.* Milwaukee, July 8-10. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., 1 West Wilson St., Madison.

Wyoming: *Examination and Reciprocity.* Cheyenne, Oct. 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

Alaska:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Guam: *Subject to Call.* Act. Sec., Dr. S. F. Provencher, Agana.

Hawaii: *Examination.* Honolulu, July 14-15. Sec., Dr. I. L. Tilden, 1029 Kapiolani St., Honolulu.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alaska: *Examination.* Juneau, Nov. 4. Sec., Dr. R. Harrison Leer, Room 204, Alaska Office Bldg., Juneau.

Arizona: *Examination.* Tucson, June 17. *Reciprocity.* Tucson, June 27. Sec., Dr. Herman E. Bateman, University of Arizona, Tucson.

Arkansas: *Examination.* Little Rock, Oct. 6-7. Sec., Dr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.

Colorado: *Examination and Reciprocity.* Denver, Sept. 3-4. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Connecticut: *Examination and Endorsement.* New Haven, June 14. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

Iowa: *Examination.* Des Moines, July 8. *Reciprocity.* Des Moines, July 7. Sec., Dr. Elmer W. Hertel, Waverly.

Michigan: *Examination.* Ann Arbor and Detroit, Oct. 10-11. Sec., Mrs. Anne Baker, 116 Stevens T. Mason Bldg., W. Michigan Ave., Lansing 15.

New Mexico: *Examination.* Santa Fe, July 20. *Reciprocity.* Santa Fe, June 26. Sec., Mrs. M. Cantrell, P. O. Box 1522, Santa Fe.

Oklahoma: *Examination and Reciprocity.* Oklahoma City, Sept. 26-27. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

Oregon: *Examination.* Portland, June 7. Sec., Dr. Earl M. Pallett, Box 5175, Eugene.

Tennessee: *Examination.* Memphis, July 1-2. Sec., Dr. O. W. Hyman, 62 S. Dunlap St., Memphis.

Texas: *Examination.* October. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Wisconsin: *Examination. Madison,* Sept. 19. Sec., Mr. William H. Barber, 621 Ransom St., Ripon.

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*Basic Science Certificate required.

GOVERNMENT SERVICES

AIR FORCE

Consultants Visit Medical Installations.—Three national consultants to the surgeon general recently visited Air Force medical installations in Europe and in the Pacific. They rendered advice on problem cases in their specialties and conducted lectures and teaching sessions at medical installations. Dr. Clair M. Kos, professor of otolaryngology, State University of Iowa, visited installations in Japan, Korea, Okinawa, Taiwan, Hawaii, and the Philippine Islands. Dr. Carlos G. deGutierrez-Mahoney, neurosurgeon at St. Vincent's Hospital in New York City, and Dr. Frank E. Stinchfield, director, orthopedic service, Columbia-Presbyterian Medical Center, New York City, visited installations in Germany, France, Tripoli, Morocco, and England.

New Hospital in Indiana.—A U. S. Air Force Hospital at Bunker Hill Air Force Base, Peru, Ind., was completed on Jan. 30. This 50-bed hospital on a 100-bed chassis is a single story, air-conditioned structure of concrete, stone, and steel, with private and semiprivate rooms, four-bed and eight-bed wards, obstetric and gynecologic service, surgical service, laboratory, pharmacy, outpatient clinics, and dental clinic. Oxygen is piped throughout the wards and rooms. Patients may choose one of four radio programs by plugging speakers or headsets into the wall next to their beds.

PUBLIC HEALTH SERVICE

First National Conference on Air Pollution.—Appointment of a committee to help plan a national conference on air pollution has been announced by the surgeon general. The national conference, first of its kind, will be held in Washington, D. C., Nov. 18 to 20, and will involve a full-scale review of current knowledge about the causes and effects of community air pollution, Dr. Burney said. The groups represented on the committee are:

Air Pollution Control Association
American Chemical Society
American Industrial Hygiene Association
American Iron and Steel Institute
American Medical Association
American Meteorological Society
American Municipal Association
American Petroleum Institute
American Public Health Association
Association of State and Territorial Health Officers
Automobile Manufacturers Association
Council of State Governments
Edison Electric Institute
Engineers Joint Council
Interdepartmental Committee on Air Pollution
Manufacturing Chemists' Association
National Advisory Committee on Community Air Pollution
National Coal Association

April Award for Research.—Research grants and fellowships totaling $5,725,219 were awarded during the month of April by the National Institutes of Health. Scientists and institutions throughout the nation received 334 research grants totaling $5,066,831. Sixty per cent of this amount supported research in the neurological diseases and mental health fields. The grants were made to 165 institutions in 38 states, the District of Columbia, 2 territories, and 5 foreign countries. The research fellowships were awarded to 149 individuals for study in 79 institutions in 27 states, the District of Columbia, and 8 foreign countries.

Twenty U. S. scientists were awarded fellowships for study abroad, while six scientists from other countries will receive research training at medical research centers in the United States of their own selection. (The six fellowships to scientists from other countries included in the April listing are among a group of 13 previously announced April 25.) Research grants are awarded to nonfederal research institutions for the support of research projects in the health sciences. Research fellowships support predoctoral and postdoctoral individuals interested in obtaining appropriate training for a research career.

Grant for Research on Aging.—The Public Health Service has made a grant of $417,939 to the Albert Einstein College of Medicine of Yeshiva University, New York City, for research on the medical and biological aspects of aging. Work to be carried on under the new grant, announced by the surgeon general during a ceremony at the university, will include (1) studies of changes that occur with age in the circulatory, nervous, and respiratory systems; (2) research training through 10 post-doctoral fellowships; each fellow to work with scientists in the new research unit, or with other faculty members engaged in research on aging; and (3) teaching, through the facility of a 90-bed ward service at the neighboring Van Etten Hospital to be established in cooperation with the city of New York.

The National Advisory Heart, Mental Health, and Arthritis and Metabolic Disease Councils recommended the grant. Although the Albert Einstein College of Medicine now has a research program on aging, the Public Health Service grant will establish a distinctly new program which will be supervised by the college's committee on gerontology.

This is the second grant in the Public Health Service's new program to encourage comprehensive research in the field of aging. The program is administered by the Public Health Service's Center for Aging Research, established in 1956, at the National Institutes of Health, Bethesda, Md., under the direction of Dr. G. Halsey Hunt. The first grant was awarded to Duke University, Durham, N. C., in August, 1957.

DEATHS

Alexander, Jewell Clyde, Livingston, Texas; University of Texas School of Medicine, Galveston, 1918; specialist certified by the American Board of Urology; member of the Texas State Medical Association and the American Urological Association; practiced in Houston, where he was professor of clinical urology at Baylor University College of Medicine; president of the Polk County Medical Society; veteran of World Wars I and II; member of the staffs of the St. Luke's Episcopal and Memorial hospitals in Houston; died March 23, aged 66.

Bolend, Rex George ✦ Little Rock, Ark.; St. Louis University School of Medicine, 1911; specialist certified by the American Board of Urology; member of the Oklahoma State Medical Association and the American Urological Association; veteran of World Wars I and II; at one time on the faculty of the University of Oklahoma School of Medicine in Oklahoma City; associated with the Veterans Administration Hospital; died in the Veterans Administration Hospital at Biloxi, Miss., March 23, aged 70.

Bolyn, Robert Talliaferro, Dallas, Texas; University of the South Medical Department, Sewanee, Tenn., 1901; died March 25, aged 84, of coronary occlusion.

Borders, Arthur Berry, Fort Worth, Texas; Meharry Medical College, Nashville, Tenn., 1917; died March 9, aged 69, of a self-inflicted gunshot wound.

Brantley, Thomas Boykin, Hilltonia, Ga.; University of Georgia Medical Department, Augusta, 1912; died in the Central of Georgia Railway Hospital, Savannah, March 24, aged 75.

Brumfield, Daniel Clyde, Darrow, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1900; member of the Louisiana State Medical Society; for many years Ascension Parish coroner; died in the Baton Rouge (La.) General Hospital March 23, aged 87, of acute pyelonephritis with abscesses, bilateral nephrolithiasis, subacute myelogenous leukemia, and injuries received in a fall.

Davis, William Cole, Lexington, Va.; University of Maryland School of Medicine, Baltimore, 1908; specialist certified by the American Board of Psychiatry and Neurology; veteran of World War I; resigned from the regular Army in 1920; commissioned a colonel and served as post surgeon at the Virginia Military Institute during World War II; formerly associated with the Norristown (Pa.) State Hospital; died in Caracas, Venezuela, Feb. 23, aged 75, of cancer and pneumonia.

Erwin, John Joseph ✦ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1920; specialist certified by the American Board of Obstetrics and Gynecology; chief of obstetrics at Mercy Hospital; on the staffs of Hospital for Women and Bon Secours Hospital; died March 14, aged 65, of arteriosclerotic cardiovascular disease.

Farrall, Byron Huntley, Groton, Mass.; Boston University School of Medicine, 1926; veteran of World War I; died in the Community Memorial Hospital, Ayer, March 14, aged 60, of coronary disease.

Foley, Sydney Ira ✦ Flint, Mich.; M.B., 1914, and M.D., 1919, Queens University Faculty of Medicine, Kingston, Ontario, Canada; specialist certified by the American Board of Radiology, Inc.; member of the Radiological Society of North America and the American College of Radiology; served overseas as a captain in the Canadian Army during World War I; on the staff of St. Joseph Hospital, where he died March 12, aged 66, of cancer.

Freeman, David Barnard ✦ Moline, Ill.; State University of Iowa College of Medicine, Iowa City, 1910; fellow of the American College of Surgeons; member of the Aero Medical Association; past-president of the Rock Island County Medical Society; veteran of World War I; on the staffs of the St. Anthony's Hospital in Rockford and the Moline Public Hospital and the Lutheran Hospital, where he died March 13, aged 71, of pyloric obstruction secondary to carcinoma of the pancreas.

Fullerton, Oscar Lewis ✦ Redding, Iowa; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1902; died Feb. 12, aged 81, of heart disease.

Gerlough, Robert Jacob ✦ Menlo Park, Calif.; The General Medical College, Chicago, 1924; died in Palo Alto March 23, aged 65.

Griffis, Lawrence Glenn, Kalispell, Mont.; Indiana University School of Medicine, Indianapolis, 1910; an associate member of the American Medical Association; veteran of World War I; died March 15, aged 70.

Haldy, Walter Alfred ✦ Brunswick, Ohio; Western Reserve University Medical Department, Cleveland, 1902; died in Millersburg March 22, aged 79.

✦ Indicates Member of the American Medical Association.

Hamilton, Gordon Battelle, San Francisco; University of the South Medical Department, Sewanee, Tenn., 1905; College of Physicians and Surgeons, Boston, 1906; veteran of World War I; served with the city health department and as health officer of Contra Costa County; died March 19, aged 81, of coronary occlusion.

Hansen, Arthur Franklin ⊕ Borger, Texas; University of Oklahoma School of Medicine, Oklahoma City, 1925; past-president of the Hutchinson County Medical Society; served as a member of the board of directors of Panhandle State Bank; veteran of World War I; president of the staff of the North Plains Hospital, where he died March 16, aged 61, of nephritis and uremia.

Heald, John Emerson, Glendale, Calif.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1903; served as medical director of the Kansas Sanitarium in Wichita; formerly associated with the Battle Creek (Mich.) Sanitarium; died in the Glendale Sanitarium and Hospital March 13, aged 77, of coronary thrombosis.

Heineck, Aime Paul, Chicago; Northwestern University Medical School, Chicago, 1896; at one time on the faculty of his alma mater; served on the staffs of the Walther Memorial, Passavant Memorial, and Jackson Park hospitals; from July, 1913, to 1927 consulting editor in general surgery of the staff of the *International Abstracts of Surgery, Gynecology and Obstetrics;* died in St. Luke's Hospital April 8, aged 88, of cancer of the bladder and arteriosclerosis.

Hengstenberg, Hugh Herbert ⊕ Madeira, Ohio; University of Cincinnati College of Medicine, 1925, member of the staffs of St. Elizabeth Hospital in Covington, Ky., Speers Memorial Hospital in Dayton, Ky., Good Samaritan, Bethesda, and Deaconess hospitals in Cincinnati; for many years company physician for the Cincinnati Gas and Electric Company; died in the Good Samaritan Hospital, Cincinnati, March 27, aged 57, of injuries received in an automobile accident.

Hobbs, Clarence Lowell, Collinsville, Ill.; St. Louis College of Physicians and Surgeons, 1922; Kansas City (Mo.) College of Medicine and Surgery, 1922; member of the Missouri State Medical Association; died in the Missouri Baptist Hospital, St. Louis, March 23, aged 73, of arteriosclerotic heart disease and cancer of the prostate.

Hufford, Clarence Elton ⊕ Toledo, Ohio; born in Perrysburg, Ohio, Feb. 9, 1893; Western Reserve University School of Medicine, Cleveland, 1920; specialist certified by the American Board of Radiology; fellow of the American College of Physicians; past-president and secretary of the Northwestern Ohio Medical Association; past-president of the Ohio State Radiology Society, Academy of Medicine of Toledo and Lucas County, Radiological Society of North America, Ohio Division of the American Cancer Society, and the Toledo Public Health Association; member of the American Roentgen Ray Society, American College of Radiology, and the American Radium Society; in 1941 received a certificate of merit from the American Medical Association for his exhibit on bone tumors: for many years associated with St. Vincent's Hospital; died in the Indian River Hospital, Vero Beach, Fla., March 25, aged 65, of coronary occlusion.

Jinks, Clifford Herrmann ⊕ Indianapolis; Indiana University School of Medicine, Indianapolis, 1924; served overseas during Warld War I; on the staffs of St. Vincent's and Methodist hospitals; died March 14, aged 61, of glioblastoma and cerebral anoxia.

Kaufman, Alexander Spencer, Philadelphia; born in Quincy, Ill., Oct. 21, 1882; Jefferson Medical College of Philadelphia, 1904; clinical professor of otology at his alma mater; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; an associate member of the American Medical Association; a member of the board of trustees of the National Agricultural College, Farm School, Pa.; on the courtesy staff of the Germantown Hospital and on the staffs of the Jefferson Hospital and the Northern Division of the Einstein Center, where he died March 30, aged 75, of ruptured aortic aneurysm and atherosclerosis of the aorta.

Kolb, Harrison John ⊕ Oakland, Calif.; University of California School of Medicine, San Francisco, 1932; member of the staffs of Providence and Herrick hospitals and Peralta Hospital, where he died March 20, aged 52, of hemorrhage from esophageal varices and cirrhosis of the liver.

Kotkis, Alexander Joseph ⊕ St. Louis; born in Gilberton, Pa., Sept. 11, 1895; St. Louis University School of Medicine, 1921; assistant professor of clinical medicine at his alma mater, where he was physician for athletic teams for a number of years: specialist certified by the American Board of Physical Medicine and Rehabilitation; member of the American Society of Physical Medicine and Rehabilitation; veteran of World War I; at one time served as boxing physician for the Missouri State Athletic Commission; since 1932 physical therapist at St. Mary's Group of Hospitals; died in Mount St. Rose Hospital March 23, aged 62.

Koven, Abraham ⊕ Detroit; Detroit College of Medicine and Surgery, 1915; member of the American Academy of General Practice; for many years diagnostician for the city health department; on the staff of the Detroit Memorial Hospital; died in the University Hospital, Ann Arbor, March 16, aged 63, of cancer.

Lamothe, Frank Eugene ⊕ New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1908; on the consulting staff of Southern Baptist Hospital, where he died March 19, aged 74, of enterocolitis.

La Rue, Raymond T. ⊕ Wilmington, Del.; Temple University School of Medicine, Philadelphia, 1920; associated with Delaware, St. Francis, and Delaware State hospitals; died March 17, aged 62, of heart disease.

Leden, Peter Paul ⊕ Chicago; Schlesische Friedrich–Wilhelms–Universität Medizinische Fakultät, Breslau, Prussia, 1913; assistant clinical professor of otorhinolaryngology at Stritch School of Medicine of Loyola University; on the staff of St. Francis Hospital in Evanston, Ill., where he died March 31, aged 71, of myocardial infarction.

Loub, Martin Francis, Colorado Springs, Colo.; Colorado School of Medicine, Boulder, 1906; died March 15, aged 81, of bronchopneumonia.

Lynn, Frank M. ⊕ Peru, Ind.; Central College of Physicians and Surgeons, Indianapolis, 1894; formerly member of the city board of health, serving as secretary for eight years; served as city health officer; on the staff of the Dukes-Miami County Hospital; died March 17, aged 88, of uremia and heart disease.

McEwan, John Howard ⊕ Bay City, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1913; member of the American Academy of General Practice; veteran of World War I; died in the Mercy Hospital March 14, aged 68.

McNemar, Oscar Harrison, Millersville, Md.; Maryland Medical College, Baltimore, 1903; formerly associated with the Veterans Administration hospital in Rutland Heights, Mass., and Castle Point, N. Y.; died March 21, aged 85, of heart disease.

McPherson, Garland, Hillsboro, Texas; University of Tennessee College of Medicine, Memphis, 1934; member of the Texas Medical Association; veteran of World War II; served as president and vice-president of the Hill County Medical Society; died March 17, aged 49, of a gunshot wound in the head.

Maxfield, James Robert Sr. ⊕ Dallas, Texas; Fort Worth School of Medicine, Medical Department of Texas Christian University, 1901; past-president of the Van Zandt County Medical Society; received a selective service certificate of merit for his services during World War II; died March 20, aged 86, of cancer of the rectum with metastasis to the liver.

Moench, L. Mary ⊕ White Plains, N. Y.; Johns Hopkins University School of Medicine, Baltimore, 1919; formerly associated with the Mayo Clinic in Rochester, Minn.; served as a member of the medical staff at Smith College in Northampton, Mass.; fellow of the American College of Physicians; served as instructor in medicine at Cornell University Medical College in New York City; associated with the New York Hospital and the White Plains Hospital, where she died March 27, aged 66, of cancer.

Moon, William Benjamin ⊕ Crystal River, Fla.; Hospital College of Medicine, Louisville, Ky., 1897; veteran of World War I; state senator for three terms; died March 20, aged 87.

Morris, Frank Lincoln ⊕ Cass City, Mich.; Detroit College of Medicine, 1910; served as a member of the school board and health officer; died March 17, aged 72, of coronary occlusion.

Morrissey, John Joseph Jr., Baltimore; Maryland Medical College, Baltimore, 1910; died March 29, aged 73, of carcinoma of the bladder.

Moses, Harry ⊕ Palm Beach, Fla.; University of Virginia Department of Medicine, Charlottesville, 1908; fellow of the International College of Surgeons and the American College of Surgeons; associated with Good Samaritan Hospital and St. Mary's Hospital in West Palm Beach, where he died March 20, aged 76, of angina pectoris.

Newman, Adolph Jacob, Hinsdale, Ill.; Bennett Medical College, Chicago, 1910; retired from the Veterans Administration Aug. 31, 1955; for many years associated with the Veterans Administration Hospital in Hines, where he died April 4, aged 73, of coronary thrombosis.

Nill, Jacob Philip ⊕ McKeesport, Pa.; University of Pittsburgh School of Medicine, 1925; veteran of World War II; on the staff of the McKeesport Hospital; died March 22, aged 59, of acute coronary occlusion.

Nutt, John Budd ⊕ Williamsport, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1911; fellow of the American College of Surgeons; past-president of the Lycoming County Medical Society; veteran of World War I; associated with the Williamsport Hospital; died March 19, aged 73.

Ostrom, Frank Ward, Eaton, N. Y.; Hahnemann Medical College and Hospital of Philadelphia, 1904; died March 3, aged 75, of chronic myocarditis and congestive heart failure.

Peacock, Cassius Lee, New Orleans; Emory University School of Medicine, Atlanta, 1916; member of the Louisiana State Medical Society, of which he was formerly vice-president, and the American Urological Association; member of the House of

Delegates of the American Medical Association from 1944 to 1946; on the staff of the Southern Baptist Hospital; died March 16, aged 71.

Porter, Steven Alfred ⊕ Okanogan, Wash.; University of Nebraska College of Medicine, Omaha, 1929; associated with St. Martin's hospital, Tonasket; died in Seattle March 2, aged 53, of myocardial infarction.

Raiguel, George Earle, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1902; died March 29, aged 77.

Ramsey, Rolla Benjamin, Richmond, Ind; Eclectic College of Physicians and Surgeons, Indianapolis, 1893; veteran of World War I; died March 19, aged 89, of arteriosclerotic heart disease.

Ray, William Burton Getty, Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1900; specialist certified by the American Board of Radiology; an associate member of the American Medical Association; member of the American Roentgen Ray Society, Radiological Society of North America, and the American College of Radiology; veteran of the Spanish-American War and World War I; associated with the Allegheny General Hospital, where he died March 21, aged 85, of carcinoma of the pancreas.

Rieke, Arthur George, San Francisco; University of Illinois College of Medicine, Chicago, 1918; served as assistant superintendent of the San Francisco Hospital; died in Blairstown, Iowa, Feb. 22, aged 71.

Robinson, Louis Henry ⊕ Newark, N. J.; Long Island College Hospital, Brooklyn, 1906; died in Miami Beach, Fla., March 21, aged 75, of coronary disease and a cerebral accident.

Rubin, Harry, Kilgore, Texas; University of Pennsylvania School of Medicine, Philadelphia, 1912; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; veteran of World Wars I and II; formerly associated with the Veterans Administration hospitals at Augusta, Ga., Gulfport, Miss., Palo Alto, Calif., American Lake, Wash., and Waco, Texas; died in the Veterans Administration Hospital, Dallas, Texas, March 18, aged 67, of lobar pneumonia.

Rundell, William Kennard, Wichita Falls, Texas; Baylor University College of Medicine, Dallas, 1935; died in the Wichita General Hospital March 11, aged 48, of cerebral hemorrhage.

Sabin, George Millar ⊕ Burlington, Vt.; University of Vermont College of Medicine, Burlington, 1900; professor emeritus of clinical surgery at his alma mater; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; veteran of World War I; on the staffs of the Porter Memorial Hospital in Middlebury and the Fanny Allen, Mary Fletcher, and Bishop de Goesbriand hospitals: died March 21, aged 84.

Sayler, John Milton, Dayton, Ohio; Starling Medical College, Columbus, 1903; chief medical examiner for the Baltimore and Ohio Railroad in Cleveland for many years; died March 18, aged 79.

Schaeffer, Jacob H., Cridersville, Ohio; Medical College of Ohio, Cincinnati, 1891; served on the staffs of the Memorial and St. Rita's hospitals in Lima; died in St. Mary's, March 19, aged 93.

Schnur, Howard Lee ⊕ Houston, Texas; Columbia University College of Physicians and Surgeons, New York City, 1949; certified by the National Board of Medical Examiners; service member of the American Medical Association; veteran of World War II; assistant chief, department of physical medicine and rehabilitation, Veterans Administration Hospital, where he died March 22, aged 40, of cerebral hemorrhage and acute leukemia.

Selman, Willis Lee, San Antonio, Texas; (licensed in Texas, under the Act of 1907); died March 13, aged 83.

Skillin, Waldo Thompson, South Portland, Maine; Medical School of Maine, Portland, 1914; served as chairman of the board of education, health officer, and as a medical examiner; died March 18, aged 68.

Snodgrass, Thomas Joseph ⊕ Janesville, Wis.; University of Minnesota Medical School, Minneapolis, 1916; specialist certified by the American Board of Surgery; veteran of World War I; member and past-president of the Western Surgical Association; member of the American Trudeau Society; fellow of the American College of Surgeons; a founder and past-president of the Wisconsin Surgical Society; formerly member of the city council; on the staff of the Mercy Hospital; died April 7, aged 66, of injuries received in an automobile accident.

Stevens, Charles Elmer ⊕ Ironwood, Mich.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1910; served as city health officer; chief of staff, Grandview Hospital; associated with Divine Infant Hospital in Wakefield; died in the F. A. Bell Memorial Hospital, Ishpeming, March 4, aged 74, of bronchogenic carcinoma.

St. Onge, Joseph Abel ⊕ Sioux City, Iowa; Sioux City College of Medicine, 1907; on the staff of St. Vincent's Hospital; died March 17, aged 76, of coronary occlusion.

Tannenbaum, Israel Samuel ⊕ Worcester, Mass.; Kansas City (Mo.) University of Physicians and Surgeons, 1929; served as medical examiner for the Boston Mutual Life Insurance Company; for many years on the courtesy staff of the St. Vincent Hospital; died in Miami, Fla., March 20, aged 55, of acute pulmonary edema and arteriosclerotic heart disease.

Terry, George Hiram Blakeslee, Asheville, N. C.; Jefferson Medical College of Philadelphia, 1895; veteran of World War I; served with the Veterans Administration; died March 4, aged 87, of heart disease.

Tiffany, William James, New York City; born in Groton, N. Y., July 29, 1882; Columbia University College of Physicians and Surgeons, New York City, 1905; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association and the Association for Research in Nervous and Mental Diseases; state commissioner for mental hygiene from 1937 to 1943; entered the state hospital service in 1906, attached to Binghamton (N. Y.) State Hospital and Manhattan State Hospital in New York City; formerly superintendent of the Kings Park (N. Y.) State Hospital and the Pilgrim State Hospital in Brentwood; died in the Neurological Institute of the Columbia-Presbyterian Medical Center March 28, aged 75, of coronary thrombosis.

Treusch, Herbert Louis ⊕ Washington, D. C.; Emory University School of Medicine, Atlanta, 1925; service member of the American Medical Association; served as vice-president of the American Physicians' Art Association; formerly practiced in Atlanta, where he was associated with the Crawford W. Long Memorial Hospital; medical officer of the Veterans Administration Board of Veterans Appeals; died March 25, aged 57.

Turnage, Johnson Lee, Fort Walton, Fla.; Tulane University School of Medicine, New Orleans, 1942; certified by the National Board of Medical Examiners; veteran of World War II; public health director; died March 19, aged 43, of acute myocardial infarction.

Ullrich, Henry Franz ⊕ Baltimore; born in Baltimore Nov. 17, 1903; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1929; specialist certified by the American Board of Orthopaedic Surgery; member of the American Academy of Orthopaedic Surgeons; fellow and member of the board of governors of the American College of Surgeons; associate professor of orthopedic surgery at his alma mater; veteran of World War II; associated with the Franklin Square, Mercy, St. Joseph's, Maryland General, Bon Secours, University, Union Memorial, Lutheran, and St. Agnes hospitals, and Church Home and Hospital; died in the University Hospital March 24, aged 54, of lymphosarcoma.

Van Lengen, Nicholas Warner ⊕ Syracuse, N. Y.; Syracuse University College of Medicine, 1909; one of the founders and member of the board of directors of Peoples Hospital, where he died March 16, aged 71, of acute myocardial infarction.

Verity, Walter, Chicago; Rush Medical College, Chicago, 1910; veteran of World War I; served on the staffs of the Woodlawn Hospital and the City of Chicago Municipal Tuberculosis Sanitarium; died in the Albert Merritt Billings Hospital April 1, aged 83, of acute myocardial infarction.

Walker, Roger Venning Jr. ⊕ Detroit; Wayne University College of Medicine, Detroit, 1951; instructor of surgery at his alma mater; associated with Detroit Memorial and Receiving hospitals; died in the Henry Ford hospital March 19, aged 32.

Wesson, Paul D., Memphis, Tenn.; St. Louis College of Physicians and Surgeons, 1922; died March 21, aged 70, of pneumonia.

Westby, Magnus ⊕ Madison, Minn.; University of Minnesota Medical School, Minneapolis, 1927; member of the American Academy of General Practice; president of the state board of medical examiners; twice mayor of Madison; on the staff of the Madison Hospital; died in Santa Ana March 13, aged 58, of coronary occlusion.

Willhite, David Walter Jr. ⊕ La Mesa, Calif.; University of Southern California School of Medicine, Los Angeles, 1949; associated with the Paradise Valley Sanitarium and Hospital, National City; died March 9, aged 32, of an overdose of barbiturates, self administered.

Wright, Thew, Buffalo, N. Y.; born in Boston June 19, 1877; University of Buffalo School of Medicine, 1903; professor of surgery emeritus at his alma mater; an associate member of the American Medical Association; member of the Medical Society of the State of New York and the American Association of Obstetricians and Gynecologists; fellow of the International College of Surgeons and the American College of Surgeons; member of the founders group of the American Board of Surgery; veteran of World War I; formerly member of the city board of health; served on the staff of the Buffalo General Hospital; died in the Veterans Administration Hospital March 20, aged 81, of cerebral thrombosis.

Wyman, Frank Bertram ⊕ Seattle; Northwestern University Medical School, Chicago, 1950; member of the American Academy of General Practice; died in the Maynard Hospital March 9, aged 34, of coronary artery occlusion.

FOREIGN LETTERS

FRANCE

Blood Urea Levels.—Since Widal analyzed the successive steps of progressive azotemia in the course of chronic nephropathy, many physicians have relied on serum urea levels to detect renal insufficiency. Hamburger and Masson (*La presse medicale* 66:499, 1958) studied 150 unselected patients from a nephrology consultation unit. They compared the urea level with the values of the urea clearance and the glomerular clearance and found 50 mg. of urea per 100 ml. of serum to be an unreliable guide to kidney function in patients who were not examined under strict basal conditions. One may find the concentration of urea to be less than 50 mg. per 100 ml. in patients in whom more than a half of the functional value of the kidneys was already lost, and one may find levels above 50 mg. per 100 ml. in patients whose renal function was normal.

INDIA

Thoracic Injuries.—Anand and Singh (*Indian Journal of Surgery*, vol. 20, February, 1958) stated that fractures of the ribs are the commonest type of thoracic injuries in civilian practice. About 15% of patients with closed thoracic injuries, most of whom are run over by automobiles, die. The stove-in chest is almost always fatal unless prompt and proper treatment is given. The authors reported a series of 75 cases of closed thoracic injuries in which 10 patients had paradoxical respiration and 5 had stove-in chests. The complications noticed in these cases were pulmonary edema, hemothorax, tension pneumothorax, diaphragmatic hernia, and acute dilatation of the stomach. In treating ordinary fractures of the ribs, relief of pain is all that is required, and this was provided by using intercostal or paravertebral block. Five patients had blood in the pleural cavity; it was aspirated from three of these. No patient required decortication. The four patients with tension pneumothorax were treated by intercostal aspiration with a needle connected to a tube under water seal. In treating patients with stove-in chests, the surgeon may be confronted with paradoxical respirations, severe pain from fractured ribs, and excessive tracheobronchial secretion.

Of the five such patients in this series only two required an operation to stabilize the chest; both recovered. Fixation of the ribs was obtained with silk or stainless steel wire sutures without any external traction. The other three patients died, one an hour after admission due to an associated fracture of the skull, one 10 hours after admission of an associated tension pneumothorax on the same side and massive hemothorax on the opposite side, and the third 3 days after admission of pulmonary edema and acute dilatation of the stomach. Intercostal or paravertebral block was used to relieve the pain. An intravenous drip of procaine in saline solution was given if this failed. Shock was treated by transfusion of blood, dextran, and other fluids. The authors did not use tracheotomy to restore normal respiratory movements in any of these patients, but others have found an early tracheotomy to be a lifesaving measure in many patients with crushing thoracic injuries as it reduces paradoxical movements, alleviates pain by decreasing movements of the fractured ribs, and provides an easy method for aspirating the tracheobronchial tree without the need for a bronchoscope in patients with pulmonary edema.

Acetazolamide in Ophthalmology.—J. M. Pahwa (*Indian Journal Medical Sciences*, vol. 12, Jan., 1958) stated that acetazolamide, a powerful carbonic anhydrase inhibitor, lowers intraocular pressure. It has therefore been used in the treatment of glaucoma. Although the exact mechanism of its action is not known, it is believed to diminish the production of aqueous humor. It reduces the aqueous inflow by lowering the aqueous electrolytic concentration and osmotic pressure. The author tried this drug in a series of 100 patients with acute and chronic glaucoma. Complications were few, but in one patient there was epistaxis. Results were good in those with acute congestive glaucoma and secondary glaucoma due to coughing, iritis, or trauma. Two patients with chronic glaucoma were well controlled for over eight months, but, in general, the results were uncertain in chronic glaucoma. The drug was found useful in postoperative nonformation of the anterior chamber after intraocular operations where no leak could be detected, particularly in patients with detachment of the choroid. It was also of use after keratoplasty, where it helped in the prevention of noninflammatory edema of the cornea. The best results were obtained in patients with acute congestive glaucoma, especially when combined with miotics.

Anesthetic Action of Antihistaminics.—R. Goswami and co-workers (*Indian Journal of Medical Sciences*, vol. 12, February, 1958) stated that most antihistaminics, besides having a sedative action,

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The items in these letters are contributed by regular correspondents in the various foreign countries.

Tannenbaum, Israel Samuel ⊕ Worcester, Mass.; Kansas City (Mo.) University of Physicians and Surgeons, 1929; served as medical examiner for the Boston Mutual Life Insurance Company; for many years on the courtesy staff of the St. Vincent Hospital; died in Miami, Fla., March 20, aged 55, of acute pulmonary edema and arteriosclerotic heart disease.

Terry, George Hiram Blakeslee, Asheville, N. C.; Jefferson Medical College of Philadelphia, 1895; veteran of World War I; served with the Veterans Administration; died March 4, aged 87, of heart disease.

Tiffany, William James, New York City; born in Groton, N. Y., July 29, 1882; Columbia University College of Physicians and Surgeons, New York City, 1905; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association and the Association for Research in Nervous and Mental Diseases; state commissioner for mental hygiene from 1937 to 1943; entered the state hospital service in 1906, attached to Binghamton (N. Y.) State Hospital and Manhattan State Hospital in New York City; formerly superintendent of the Kings Park (N. Y.) State Hospital and the Pilgrim State Hospital in Brentwood; died in the Neurological Institute of the Columbia-Presbyterian Medical Center March 28, aged 75, of coronary thrombosis.

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Wesson, Paul D., Memphis, Tenn.; St. Louis College of Physicians and Surgeons, 1922; died March 21, aged 70, of pneumonia.

Westby, Magnus ⊕ Madison, Minn.; University of Minnesota Medical School, Minneapolis, 1927; member of the American Academy of General Practice; president of the state board of medical examiners; twice mayor of Madison; on the staff of the Madison Hospital; died in Santa Ana March 13, aged 58, of coronary occlusion.

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ing used on an ever-increasing scale. A promising activity begun in recent years is domiciliary treatment under the supervision of clinics equipped with x-ray units and laboratories.

Medical Gases.—The system of coloring cylinders of medical gas in India did not correspond with that used in many other countries. As a result accidents occurred from mistakes in identification of gases by foreign physicians or by those trained overseas. The Government has therefore amended the Gas Cylinder Rules so that the color markings of these cylinders will conform with the international system.

Nutrition of School Children.—Nutritional surveys of school children by the State Nutritional Advisory Committee showed that the main deficiency was of vitamin A. Only a few children with riboflavin deficiency were seen, and the incidence of deficiency of vitamins C and D was not high. The incidence of dental caries was about 20%. Nearly 40% of those examined had a poor physique. In most places the intake of vegetables, especially green leafy vegetables, was inadequate. Except in the western districts where ghee was taken in small quantities, the fats and oils used were usually vanaspati and mustard oil. The intake of fats derived from animal sources was low. Seasonal fruits included bananas, papayas, guavas, and mangoes but the quantities taken were small. Milk, milk products, and meat were either absent from the diet or their intake was low. The diets of these children were characterized by high intake of cereals and low consumption of protective foods.

In view of these investigations, the State's Education Department is teaching nutritional principles in schools through lectures and visual aids and has a program of midday meals in practically all the secondary schools. Puffed rice, parched gram, sprouting gram, and seasonal fruits are distributed to school children. Intensive efforts are being made to educate and persuade the villagers to have small kitchen gardens to meet their requirements of green leafy vegetables. The intake of germinated pulses is being encouraged. In certain areas, school children between the ages of 5 and 12 are given potassium iodide as a prophylactic measure against endemic goiter for 10 days in spring and autumn.

PORTUGAL

Prefrontal Lobotomy.—Nunes da Costa (*Anais Portugueses de Psiquiatria*, Sept. 9, 1957) made a follow-up survey on 197 patients who had had prefrontal lobotomy. Most of these patients (130) were schizophrenic. The survey included interviews with members of the families and working associates. In relation to the course of the mental disease, the best results of lobotomy were obtained in psychosis, with spontaneous remission. Lobotomy can arrest, for a variable time, the development of the psychosis, especially in patients with spontaneous periodic remissions; but it can neither definitively arrest nor favorably modify the eventual course. Relapses are frequent, and they are attended by the usual symptoms. Analyzing the influence of lobotomy on the patients' personality, the author found (1) concerning the process of thinking: diminution or loss of "abstraction" and of the elaboration of thinking, superficiality of the thoughts, diminution or loss of imagination and the representative capacity, diminution of attention and memory, extraversion, diminution of the capacity of synthesis, alterations of perception, and poorer grasp of language; (2) concerning affectivity: diminution of the affective reaction, emotional flattening, loss of inhibitions, superficiality of contacts, and loss of interests; and (3) concerning activity: diminution of initiative and general activity and a tendency to akinesia. Lobotomy causes a diminution of the capacity of reaction of the organism to disease in general. Mortality is high among lobotomized patients. Hunger and pain lose their vital functions of alarm. If some improvement of the psychosis is obtained this must be weighed against the disadvantages.

UNITED KINGDOM

Serum Lipids in Diabetic Children.—It is generally considered that the serum lipoprotein level rises before the development of atheroma, and in diabetics there is a tendency for arterial disease to develop prematurely, leading to occlusive coronary disease, retinopathy, and nephropathy. Wolff and Salt (*Lancet* 1:707, 1958) studied the serum lipids and lipoproteins in 35 diabetic children, who, although showing no evidence of arterial disease, are almost certain candidates for its development. The mean levels of beta-lipoprotein, lipid, cholesterol, and esterified fatty acids in the serum were significantly higher in the children with blood sugar levels above 200 mg. per 100 ml. than in those with lower levels. As the blood sugar level rose so did that of the serum beta-lipoprotein. In three children with moderate or slight ketosis, whose diabetes had never been treated, the serum lipid level was high, the rise being mainly in the beta-lipoprotein fraction. After treatment with insulin, the fall in blood sugar level was accompanied by a corresponding fall in the serum beta-lipoprotein level. In two patients it was reduced to normal in one or two days.

One child, with long-standing diabetes, admitted in coma, had a high level of serum total lipid and beta-lipoprotein. She recovered, but gangrene and peripheral neuritis developed. The serum lipoprotein and blood sugar levels were still within normal limits several months later, although complications were still present. In this case the serum lipid abnormality preceded the development of arterial disease but remained reversible with insulin treatment. These observations supported the shown little response to speech therapy, were selected for treatment. They were seen at intervals of one week during active treatment and later at intervals of one month for a total period of eight months. They were given 400 mg. of meprobamate three times a day. An excellent result was obtained in six patients, a good result in eight, and little or no improvement in four. An excellent result was considered to be one in which the extent of improvement was such that speech difficulty appeared only during exceptional emotional tension. A good result was considered to be one in which subjective and objective improvement permitted satisfactory employment, with intermittent speech hesitancy. Inert control tablets were used in the treatment of eight patients, but only two claimed some subjective benefit. Meprobamate interrupts the vicious circle of tension, speech inhibition, and consequent anxiety in those who stutter, makes patients more accessible to speech therapy, and enables better results to be obtained in suitable cases than the application of standard methods over a longer period.

Cancer Statistics.—The General Register Office summarized cancer statistics for England and Wales from the beginning of the century to the present (McKenzie, A: Cancer Statistics for England and Wales, 1901 to 1955, Her Majesty's Stationery Office). In the last 20 years the total mortality from cancer of all sites increased for men at every age, but it decreased among middle-aged women. This difference between the two sexes is largely due to the much higher incidence of cancer of the lung in men. The commonest sites for cancer, causing death in the period 1950 to 1954 were, for men, lung (336 per million population), stomach (211), intestine (109), rectum (88), and prostate (74). For women the figures were breast (182), stomach (118), uterus (91), ovary (60), and intestine (6). About 1% of those dying of cancer were children under 15, and over half of these deaths were due to diseases of the blood-forming organs. There were regional differences in death rates from cancer. Thus in Wales the mortality from cancer of the esophagus was high, while that of cancer of the lung was low. The North of England had a high mortality from cancer of the stomach. The effect of industrialization on cancer of the lung was apparent, the incidence being higher in large industrial areas. On the other hand the death rates from cancer of the pancreas, kidney, and bladder were relatively higher in Southern England than elsewhere.

Press Not Admitted to Broadcasts.—The Council of the British Medical Association decided not to admit representatives of the lay press to the clinical demonstrations to be televised at the annual meeting of the Association in Birmingham. They will be admitted only during the televising of surgical operations. The council was asked to allow the press to be present during the whole program, but it rejected this request as it thought that only the most sensational aspects of the clinical cases were likely to be reported.

Food Poisoning due to Clostridium Welchii.—McNicol and McKillop (*Lancet* 1:787, 1958) reported an outbreak of food poisoning due to Clostridium welchii in a Glasgow hospital. Nine of 15 patients and a kitchen maid were affected after eating cold chicken. These patients were on a special light diet. Others in the same ward on ordinary diet were unaffected. The maid was taken ill after eating leftover chicken. Rectal swabs from all 16 persons were taken and nonhemolytic heat-resistant Cl. welchii isolated from 11. The identity of all the cultures was confirmed by demonstration of the fact that they produced Cl. welchii α-toxin and that was specifically neutralized by α-antitoxin. The clinical findings were typical. About eight hours after the precooked chicken was eaten, there was a brief illness characterized by colicky lower abdominal pain and watery diarrhea, without mucus, blood, or pus. Pyrexia was absent and systemic upset minimal.

Scotland's Health.—The Department of Health for Scotland reports that while the death rate was falling in all other groups, in men in the second half of life it was rising. This rise was not due to the increase in the average age of the population but to an increase in morbidity. The report states that at and beyond middle age there were few causes of death that did not affect men more than women. The chief cause of increased male mortality was the greater incidence of cardiovascular and pulmonary disease in aging men. If it were not for these illnesses the male death rate would be close to that of the female. The mortality of men aged 55 to 64 from all causes increased in Scotland in the last decade, yet in England and Wales it remained more or less stationary in this age group, although the rate in men over 65 increased. In women of 75 and over the death rate was fairly constant in the last decade and decreased in all other age groups. Infant mortality continued at a low rate. Deaths from tuberculosis were 13 per 100,000 population, compared with 66 10 years ago, but reported cases of tuberculosis increased from 5,915 in 1956 to 7,859 in 1957, not because of an absolute increase in the incidence of this disease but from improved case-finding with the help of mass roentgenography. In the 1957 drive 1,319,867, or about 20% of the population, were x-rayed. The chief cause of death after cardiovascular disease and cancer was accident. Bronchitis was the fifth on the list as the cause of death and was responsible for most absence from work. Influenza took its toll of 90 deaths in one week, although on the whole this condition was relatively benign over the year. The state of children's teeth caused some alarm. Dental examinations revealed that 20 to 30% of the teeth of children aged 12 were missing, decayed, or filled.

Cost of National Health Service.—The National Health Service, 10 years old this July, has proved far more expensive than was originally contemplated, even taking into account the rise in prices and the fact that people are living longer. The gross cost of the service has increased from 1,225 million dollars in 1949-1950 to 2,083 million dollars yearly. This is an increase of 70%. The expenditure represents 3.7% of the country's total income. The personnel employed in the health service has increased. In the last 10 years the number of nurses has gone up from 148,812 to 181,470, and medical and dental staff in the hospitals has increased from 11,940 to about 17,000. Administrative and clerical staff have expanded from 25,117 to 32,000. There are also 2,000 more general practitioners than 10 years ago. There has been an increase in the number of hospital beds, from 448,057 to 476,870, and 800,000 more inpatients were treated in the last year than in 1949. Outpatient attendances went up from 26 million a year to nearly 28 million, and free domiciliary specialist consultations from 129,500 to 265,000. Prescriptions increased from 202 million in 1949 to nearly 229 million and the number of dental treatments from 6,768,000 to 8,619,000. Only for false teeth and spectacles was there a decline.

The rise in cost of the health service is due to an increase in the services offered, rising prices including salaries and wages, a rise in the population, and an increase in the number of the aged, who need more medical attention than the young. An average of about $3 a week of health service funds are now spent on each family. Undoubtedly the expenditure on the hospitals dwarfs all other items. The drug bill, about which so much is heard, has not increased any more since the inception of the service than the other items. At the outset the hospitals received half the total allocation of money for the service. Now they receive 57% as against 9.8% for general practitioner services. The cost of drugs was more than the general practitioners received for prescribing them. In the hospitals the payments to physicians were only 9% of all hospital expenditure and were less than the cost of the patient's food (11% of the total). The estimated total budget for 1958-1959 is $1,907,668,774, of which hospital, specialist, and ancillary services represent $1,223,845,765. In the new budget the hospital services account for more than 60% of the total.

Increased Radioactivity.—The radioactivity over London is measured daily by Kodak Ltd. as part of their control over the manufacture of photographic film. An increase was recently detected, reaching a peak on March 24, when it was 10 to 20 times the normal. After the accident at Windscale, when radioactive iodine escaped into the air, it was 100 times the normal figure. The Atomic Energy Authority confirmed that there has been a small but sharp temporary increase in radioactivity over Great Britain in the second half of March. The increase of radioactivity, which was due to short-lived fission products, is assumed to be the result of recent atomic bomb explosions in Soviet territory.

Duke of Edinburgh President-Elect of British Medical Association.—His Royal Highness Prince Philip, Duke of Edinburgh, accepted the invitation of the British and Canadian Medical Associations to be their president for 1959-1960. Both associations will hold a joint meeting in Edinburgh in July, 1959. This is a return visit of the joint meeting held in Toronto in 1955. This is the first time that a member of the royal family has accepted the position of president of the two associations. Prince Philip became an honorary member of the B. M. A. in 1954. King Edward VII, when Prince of Wales, was made a member in 1900. In 1859, Prince Albert, Queen Victoria's consort, gave the inaugural address as president of the British Medical Association.

Chair of Pediatric Surgery.—Mr. A. W. Wilkinson's appointment to the London University chair of pediatric surgery is the first such appointment in Great Britain. It was established in honor of Lord Nuffield's 80th birthday by the Nuffield Foundation, which has contributed $225,000 for the purpose.

Doctors' Sons not Entering Medicine.—In evidence before the Royal Commission on Doctors' and Dentists' Remuneration, Professor A. M. Claye, said that many physicians are dissuading their sons from entering the profession of medicine because of the lack of financial incentive and added that a different type of person is now taking up medicine as a career. Fewer young physicians now come from the professional classes, and particularly from doctors' homes. This may or may not be a bad thing, but it shows that the professional classes regard medicine as a less satisfactory career than they did formerly. If this is so, it should be viewed with misgiving. The tradition of service and sense of vocation, so essential to the practice of medicine at its highest level, are less readily acquired by those brought up in homes without this background. On the other hand, there is as yet no evidence that the academic standards of the newly rible." Some said it was their practice to use in its place such expressions as "scout film" or "plain film." The oldest of the group, Dr. William Newcomet,[11] said he had never known what it meant. Said he:

> As my work in the x-ray field began in 1898, my ideas might be considered just a little "old fashioned" [but] I still try to keep up in a general way. . . . The request for a "flat film of the abdomen" does not seem unusual and I believe it is frequently used. However, when such a request [was made] to me an effort was made, to find out exactly what was expected, and the examination conducted accordingly.

Inquiry was made of 16 other outstanding American radiologists. All replied, and all had more or less definite opinions about the meaning of the phrase. Twelve of them thought it meant just one thing. Five of these thought it meant "taken with the patient horizontal," and three specified "facing the tube." Three of the 12 said it meant "not stereo."

Meanings Assigned to "Flat Film of the Abdomen" by Sixteen Leading American Roentgenologists

Patient's Position	Stereoscopic	Contrast Medium	Alternative or preferred terms
...	...	None	Plain film
Any	...	None	Preliminary film, plain film
Any	...	None	Scout film
Any	...	None	Scout film
Horizontal*	...	None	Plain film, scout film
Horizontal	No	None	
Supine	...	...	KUB film
Recumbent, AP	...	...	Scout film
Supine (facing tube)	...	Yes or no	Preliminary film
Prone or supine	...	...	AP or PA film
Supine	**No**	None	Scout film; KUB film
Supine	Yes or no	Yes or no	
PA or AP	**No**	...	Survey film
...	No	...	Scout film
.	No	...	Exploratory film; scout film
upine (usual meaning)	**No (original meaning)**	Yes or no	

*Where more than one meaning was given, the meaning stated to be primary or essential is in bold-face type.

Four said it meant "taken without artificial contrast medium." Three of the most forthright and confident replies received[12] were in this latter group.

Three others (seven in all) also voted for "no contrast medium," two decisively and one by saying "some think it also means." One of these three said it also meant "patient horizontal," one said it meant "patient horizontal, and not stereo," and one said it also meant "patient supine, and not stereo." Just one correspondent—who said its original meaning was "not stereo" though it was now often taken to mean "patient supine"—said it did not imply "without contrast medium"! In addition to the three who thought "not stereo" the sole meaning of "flat film," three others included this as a part of their definition of the phrase.

Five thought "horizontal position," variously expressed, was the sole meaning of "flat film," and five others made it a part of their definition. Two said merely "horizontal," one said "PA or AP," and one said "prone or supine;" but four specified "supine" and two specified it indirectly, one by saying "AP" and the other by saying "facing the tube."

Summary

Sixteen outstanding American radiologists were asked to define the term "flat film." The horizontal position received 10 votes, "no contrast medium" 7 votes, and "not stereo" 6 votes, a total of 22 meanings divided among 16 men, of whom 12 chose only one of the three possible meanings, and only two chose all three (see table). It seems clear from this that it would be difficult, if not impossible, to secure general agreement on the meaning of the expression "flat film of the abdomen." It is hopelessly ambiguous and should really be abandoned in casual use as it has been in roentgenologic writings.

Thirteen of the 16 radiologists queried suggested other terms; "scout film" was recommended by 7 and "plain film" by 3. Other terms (see table) were "preliminary film," "KUB," "survey," "exploratory," or "AP or PA." It is suggested that either "scout film" or "plain film" of the abdomen would be generally understood to mean a single (nonstereoscopic) roentgenogram of the abdomen in an unprepared patient and that to either of these phrases should be added a qualifying designation of position: supine (for posterior structures, equivalent to the "KUB"), prone (for the anterior abdomen), upright, or lateral.

Would we had all been as perceptive, and skeptical, as Dr. Newcomet. "Flat film of the abdomen" means, as Frederick O'Brien[13] remarked, "all things to all men." *Requiescat in pace!*

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THE LEISURE CORNER

LET'S FLY A KITE

Kites were used by Asiatic peoples centuries ago. The Chinese flew kites, and they still do, for fun, at festivals, and to keep evil spirits away from their homes. While the kite is often considered to be a toy, it has many more uses than amusing the flyer on a clear, breezy day. Ancient armies employed kites to hoist men aloft to observe operations behind enemy lines, over hills, or inside forts. Trains of kites have been used in comparatively modern times to lift men. Kites have also been used to carry light cords across river chasms so that a heavier line could then be dragged over and work started on bridges or crossings. A rescue was once effected from an ice floe by dropping a line to the marooned men by means of a kite.

Scientific research has frequently been aided by kites. Almost everyone knows the famous experiment conducted by Benjamin Franklin, who brought electricity out of the sky. In 1749, kites were used by Dr. Alexander Wilson and Thomas Melville, both of Scotland, to carry thermometers into the upper atmosphere, in order to record temperature readings high above the earth. Indeed, weather observations have been made for many years by means of kites carrying small recording instruments. When airplane traffic became too heavy, the United States Weather Bureau found it necessary to stop the use of kites, partly because the wires endangered the planes and partly because more efficient methods of collecting information had been developed.

The world's record for altitude reached by kites was made at a meteorological observation point at Mount Weather, Va., on May 5, 1910, when 10 kites in a train took about eight and a half miles of wire. What a pull that wire must have had! A full crew of men and equipment had to be organized, and the operation took many hours to complete.

With such a long, distinguished history, kites still provide exciting entertainment for both young and old people. The greatest fun lies in building and flying your own kite. Such a project carries one through the stages of planning, construction, and control. In the most rapid succession you find yourself becoming an architect, contractor, and pilot.

The kite and the airplane have a great deal in common. Both stay aloft because of the movement of the air against, across, or around its surface. The airplane has a motor to pull it through and against the air by means of a propeller, thereby making its own breeze. The kite has a cord or arrangement of cords attaching it to its line, and the long string to hold it in position while the wind is pushing against its surface. Both actions hold the heavier-than-air object off the earth, overcoming the force of gravity. The wind moves parallel to the ground and tends to carry the kite along with it. The kite is tilted about a 45-degree angle halfway between the vertical and horizontal and would fly up and away with the wind were it not for the restraint of the line which resists the pull of the wind and holds the kite nearly stationary in relation to the ground.

These two forces fight it out. If the wind wins, the kite rises a little. The angle of the kite's surface increases because of the fixed bridle, affording less resistance to the wind which cannot lift it any higher. The forces have balanced when the wind and the weight and the pull of the kite and line are equal and the kite stays put. The motion of a kite is not always up and down. Kites go sideways, too. They dive, they spin, they weave, they waggle and bob. If kites are to remain steady, the angle of the kite must remain constant. A kite with a plain or flat surface will spin all over the sky unless it has a tail, and no correction from the ground can be effective. The tail acts as a drag in the wind and holds the bottom of the kite toward the earth. All the faults of a kite, especially those of balance and flight, are caused by strong winds. The stronger the wind, the harder the kite is to handle. Therefore, the most desirable time to fly a kite occurs when the breezes are not too strong.

In building a kite it is important to obtain the largest bearing surface and the lightest weight possible. Another principle to remember is never to drive nails or tacks through the stick less they split under pressure. It is important in all symmetrical kites that the opposite surface areas be the same, and all cross sticks evenly balanced. By paying attention to proper balance in weight and surface area, a kite will have the potentialities for increasing the distance it will fly.

Today, the materials used in constructing a kite usually consist of tissue paper in the case of small kites and cloth, and silk or nylon, in the case of larger kites. Cellophane and plastic, easily fastened with tape, are the best of the newer materials. Since the wood sticks of a kite must be able to withstand the pressure of the wind against the cover, pine and cypress are very good woods to use, for the grain is usually straight, and the material is light and of moderately good strength.

Many fishermen find a kite useful when they want to fish off shore and have no boat. After the kite is launched, they attach the fish line to the main kite line with a ring or a loop of thread; the fish line will be carried out over the water, and then the bait is dropped. When the fish strikes, a good jerk breaks the loop and the fisherman reels in his fish. A large kite can pull a small wagon on a smooth road, and a smaller kite is able to drag a sled on smooth ice. If you can float on your back, you can do as Benjamin Franklin did, let a kite take you across a pond or small lake. There are many novel uses for kites. This will depend on your ingenuity. You can create your own fun as you become adept in building and flying them. And if your kite winds up in a tree, just think of the fun you have had in seeing it reach that height.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Observations on Carotenemia. The Lord Cohen of Birkenhead. Ann. Int. Med. 48:219-227 (Feb.) 1958 [Lancaster, Pa.].

Yellowish pigmentation of the skin (xanthodermia) is most frequently due to jaundice, but it may also be caused by the ingestion of substances, such as picric acid, saffron, or Atabrine, or by the excessive intake of carrots or other foods containing carotenoids. If it is due to this last cause, it is usually referred to as carotenemia, but it has been described also under such terms as aurantiasis and carotenosis cutis. Carotenoids occur in all green vegetables and especially in carrots; they are also found in butter, eggs, and oranges. Their general formula is $C_{40}H_{56}O_n$; the hydrocarbons are termed carotenes, and the hydroxyl derivatives xanthophylls. Beta-carotene is the most important precursor of vitamin A. Normally, 100 ml. of blood contains 100 mcg. of carotenoid, and the ratio of xanthophyll to carotene is 2:1.

Carotenemia may be brought on by various causes. First, there is the excessive intake of carrots. The author observed 50 cases of this type in Britain, mostly during the war when people were urged to eat carrots by the Ministry of Food. In recent years a raw carrot diet to induce slimming has been a cause. Persons have been known to eat from 4 to 8 lb. of carrots daily. In these xanthodermia tended to appear after 6 to 8 months; if carrots were then omitted from the diet, the yellowish tinge faded in 2 to 6 weeks. The main sites of the pigmentation were the face (especially the nasolabial folds) and the palms and the soles. The mucous membranes and the conjunctivas were clear, and no carotene was found in the urine.

Excessive carotene in the blood can be demonstrated and distinguished from jaundice by the simple method of Greene and Blackford: Equal volumes of serum, absolute alcohol, and petroleum ether are shaken together in a test tube and left to stand. In carotenemia, the top layer of petroleum ether shows a yellowish discoloration. In jaundice, it is in the middle layer of alcohol that the bile pigments are dissolved, and these often color also the bottom layer of precipitated proteins. Carotene often rose to 500 mcg. per 100 ml. of blood in this group of cases.

Carotenemia is observed also in patients with diabetes mellitus. It is believed that 2 factors are active in these cases: excessive intake and hyperlipemia. Other hyperlipemic states, such as nephrotic syndromes, hypercholesteremic lipoidoses, and hypothyroidism, have been known to be accompanied by hypercarotenemia. In this connection the author comments on carotenemia in patients with myxedema and on carotene and thyroid function. An inborn error in metabolism, in which there exists a defective conversion of carotene into vitamin A, is mentioned as another cause of carotenemia. The history of a woman is cited to illustrate this condition. The evidence that this patient's hypercarotenemia was due to failure of conversion of carotene into vitamin A is summarized as follows: (1) absence of excess of carotene from the diet; (2) persistent hypercarotenemia with low carotene intake over several years; (3) normal blood lipids; (4) vitamin A deficiency, although absorption of vitamin A was normal; and (5) carotene content of the serum constantly greater than its xanthophyll content. What appeared to be primarily a hypercarotenemia was accompanied by a moderate degree of hypothyroidism.

Thesaurosis Following Inhalation of Hair Spray: A Clinical and Experimental Study. M. Bergmann, I. J. Flance and H. T. Blumenthal. New England J. Med. 258:471-476 (March 6) 1958 [Boston].

The authors report on 2 women, aged 27 and 22 years, respectively, who had had previous roentgenologic examinations of the chest with completely normal findings. Both patients were free of respiratory signs or symptoms, but in both a routine x-ray examination of the chest revealed diffuse bilateral pulmonary infiltrates and hilar lymphadenopathy. This roentgenographic appearance of the chest suggested that inhalation of a noxious agent might be the cause of the lesions. To anyone who has seen hair-spray users envelop themselves in great clouds of mist, often spraying the hair above the forehead in such a manner that the spray is directed straight at the nose and mouth, there can be no question that considerable inhalation

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The place of publication of the periodicals appears in brackets preceding each abstract.

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might occur in some cases. Both patients had had the habit of spraying their hair twice daily for about 2 and 3 years respectively. Microscopic examination of tissue could be carried out in the case of only 1 patient, from whom a scalene lymph node was excised. The lesion found, although superficially resembling sarcoidosis, was distinctly different from it on histological grounds, showing a foreign-body granuloma typical of those produced by the parenteral introduction of macromolecular substances.

The only fractions of hair spray that need to be seriously considered as capable of granuloma formation are the resinous substances and lanolin. Lanolin could conceivably give rise to a lipid pneumonia, but the histological appearance of such a process would have differed from that found in the patient. Hair spray of a well-known brand was allowed to evaporate to dryness. The residue was suspended in sterile isotonic sodium chloride solution, and varying amounts of this suspension were then injected subcutaneously into the inguinal regions of 3 guinea pigs. The injected hair-spray residue acted like a typical macromolecular substance. It brought about a granulomatous inflammation at the site of the injection, and it was detected in the reticuloendothelial cells of the liver and spleen. An inflammatory reaction, which was probably due to the presence of the material in reticuloendothelial cells, was also found in the lungs of 2 guinea pigs kept for 75 days. These findings lend weight to the authors' view that in all likelihood the lesions in the lymph nodes and lungs of the 2 patients were due to the inhalation of macromolecular substances contained in hair spray. In both patients the roentgenographically visible lesions disappeared about 3 months after discontinuation of the use of hair spray.

The Etiology of Common Respiratory Infections in a Civilian Adult Population. H. G. Grieble, G. G. Jackson, H. F. Dowling and others. Am. J. M. Sc. 235:245-260 (March) 1958 [Philadelphia].

Acute respiratory infections were studied in 62 men and 60 women, between the ages of 18 and 56 years, working in clerical, technical, or professional positions in a large city. The disease was ascribed to influenza viruses in 10 patients, beta-hemolytic streptococci in 7, and adenoviruses in 4. The disease was serologically compatible with infectious mononucleosis in 2 patients, and a clinical diagnosis of Coxsackie virus infection was made in 6 patients. Thus, the acute respiratory infections were caused by unknown or undetected agents in 93 patients (75%), by known viruses or presumably caused by viruses in 22 (19%), and by hemolytic streptococci in 7 (6%). Twenty-nine of the 122 patients had fever. Sixty-three (52%) of the patients had afebrile illnesses, the causation of which was unknown and the predominant symptom of which was acute coryza or sore throat. In 27 patients (22%) the acute respiratory disease was characterized by pharyngitis with fever, pharyngeal exudate, or conjunctivitis.

These data show that among civilians the nonepidemic occurrence of febrile acute respiratory disease, pharyngoconjunctivitis, and nonbacterial exudative pharyngitis was infrequently caused by adenoviruses. The authors' findings thus suggest that immunization with adenovirus vaccine would not substantially reduce acute respiratory diseases in a civilian population. Influenza viruses, types A, B, or C, caused 25% of the febrile illnesses. Bacterial species other than hemolytic streptococci that are considered potentially pathogenic for man were most common among patients with febrile acute respiratory disease and conjunctivitis, but their causative importance was considered doubtful. The differentiation of common respiratory infections into distinct clinical syndromes has valuable diagnostic and therapeutic implications. The clinical identification of streptococcic pharyngitis was made in 60% of bacterial infections, while that of specific agents was made in only 20% of viral infections. The latter was little better than chance.

SURGERY

Results of Operations on Patients with Fibrous Dysplasia of Bone. K. Chiari. Wien. med. Wchnschr. 108:149-151 (Feb. 15) 1958 (In German) [Vienna].

The author reports on 4 female patients with fibrous dysplasia of bone, who were operated on at the ages of 41, 17, 10, and 8 years, respectively, at the first surgical clinic of the University of Vienna. The typical findings in this disease are cystic transparencies in the bones; these are unilateral in most patients. The onset of the disease takes place in early childhood; the disease progresses during infancy and usually remains stationary at the time of puberty. The bones are somewhat sclerosed in the areas adjacent to the cysts. The anatomicopathological examination reveals that the transparencies visible in the roentgenogram are pseudocysts filled with fibrous tissue.

The 41-year-old patient was operated on after her condition had remained stationary, and firm bony repair was obtained with the aid of a subtrochanteric and supracondylar osteotomy of the femur. There was delayed callus formation which, however, was not considered abnormal since the sclerosed bone appeared to be very thin subtrochanterically at the site of the osteotomy and the fibrous dysplasia may not have been responsible for this finding. The 17-year-old patient was operated on twice. At the first operation at the age of 10 years, when her disease was still progressive, the patient showed precocious puberty, and roentgenologic examination revealed coxa vara of 80 degrees for which a subtrochanteric osteotomy was performed; a cyst was not demonstrated roentgenologically in the area of the osteotomy, and bone repair was normal. Seven years later the patient had a minor accident, in which a fracture of the femur occurred, for which she was treated elsewhere by a plaster cast. Bone repair was unsatisfactory, and repeated roentgenograms showed involvement of the entire left half of the skeleton by cysts. Repeated osteotomy of the fractured bone resulted in a completely normal bone repair.

The 2 other patients were operated on directly in the cystic area. The 10-year-old patient, with severe deformity of the right lower extremity, pronounced asymmetry of the cranium, scoliosis, precocious puberty, and conspicuous pigmented nevi of the skin, was treated by osteotomy of the right femur; apparently strong callus formation resulted in clinical firmness and stability, while the roentgenogram showed a high degree of atrophy and disintegration of the bone in the area of the osteotomy. In the 8-year-old patient, with a monostatic form of fibrous dysplasia of the left femur, the osteotomy was followed by pseudarthrosis, and reoperation revealed transformation of the entire trochanter region into a soft spongy bone mass. This, however, was able to assume a normal form and almost normal structure as a result of fixation of the limb in a plaster cast for 1 year and immobilization for 6 months, after which walking exercises were started.

As a rule, surgical correction should be performed as rarely as possible in the progressive stage of fibrous dysplasia of bone, and the operation, when necessary, should be performed in an area of the bone which is roentgenologically healthy and in which normal growth of bone and bone repair may be expected. To prevent deformities, prophylactic support of the lower extremity by removal of load is indispensable. It could be assumed that a small rupture of a cyst would exert an effect similar to surgical intervention in the area of the cyst and would, therefore, cause an exacerbation of the disease. It was possible to carry out simple correction of position in all patients in the inactive stage of the disease, after the condition became stationary, and the callus formation was considered to be normal.

Imperforate Anus. E. J. Donovan and E. G. Stanley-Brown. Ann. Surg. 147:203-213 (Feb.) 1958 [Philadelphia].

The authors review observations on 21 infants and children with imperforate anus, who were observed over the 10-year period from 1946 to 1956, and all except 1 of whom were cared for by the authors. They describe the embryology and anatomy of imperforate anus and differentiate 4 types of this deformity. Type 1 is a stenosis of the anus or lower rectum, which is actually an incomplete or partial perforation; type 2 consists of a persistant thin anal membrane; type 3 is the most common form reported, and in this deformity the rectum terminates as a blind pouch ending at a variable distance from the perineal skin; in type 4, the rarest variety, both the anal canal and the lower rectum end as blind pouches which do not communicate and the distance between the 2 structures is variable. More than one-half of the patients in this report were girls with type 3 imperforate anus with associated rectovaginal fistula. The term "posterior vaginal anus" describes this most common form seen in female infants and children. The anal opening in these patients looks much like a normal anal orifice except that it is in the posterior part of the vaginal wall and is surrounded by mucous membrane instead of skin.

There were 9 male and 12 female patients; 4 died, and 2 were not operated on. Three had type 1, 2 had type 2, and 1 had type 4 imperforate anus. Of the 15 patients with type 3 imperforate anus, 11 were girls with associated rectovaginal fistula or, as the authors prefer to call it, posterior vaginal anus. In this form a perineal operation is undertaken, preferably at 4 or 5 months and certainly before the menarche. In a newborn infant, surgery should be delayed for at least 48 hours to allow time for recognition of associated congenital defects. The external anal sphincter develops independently, arising from regional mesoderm at the site of the anal dimple, and has no relation to the hind gut. It is essential to determine the exact location of the external anal sphincter in order to perform a satisfactory anoplasty. Excision of the coccyx is never indicated.

In older children with posterior vaginal anus, a secondary megacolon often develops. This should be decompressed with a proximal colostomy before initiating definitive correction of the congenital anal defect. A completely divided transverse colostomy located in the right upper quadrant functions best and leads to the fewest complications. The authors prefer the Devine type of double-barreled colostomy with complete separation of the stomas by a bridge of fascia and skin. Thorough cleansing of the intestine is essential. The surface wetting agents proved helpful in maintaining soft stools both before and after surgery. It is particularly important to cleanse adequately the distal loop of a colostomy, prior to any surgical procedure. When malnutrition accompanies imperforate anus, weight gain and improvement in general health will follow the construction of a colostomy. X-ray examination of the colon with Lipiodol, never barium, is apt to be misleading, both in regard to the presence or the absence of secondary megacolon and in the determination of distance between the anal dimple and the posterior vaginal anus. Where the opening of a posterior vaginal anus is located high up, near the cervix, a combined abdominoperineal approach is indicated. Postoperative dilatation of the new anus is a vitally important part of the treatment and must be continued by the mother. Persistent bowel training is essential.

Management of Pain Due to Pelvic Malignancy: A Follow-Up of 122 Cases. M. D. Simionescu. Zentralbl. Neurochir. 17:284-288 (No. 5) 1957 (In English) [Leipzig, Germany].

The author reports observations on 122 patients with intractable pain due to pelvic malignancy, who were treated between 1935 and 1956 at the Neurosurgical Clinic of Bucharest. The following factors may give rise to painful stimuli: (1) mechanical pressure exerted by the tumor on the pain receptors; (2) local ischemia due to arterial occlusion; (3) marked venous stasis in the pelvic viscera; (4) increased production of acid metabolites and potassium as the result of local hyperemia and tissue destructions; (5) involvement of the small arteries and their sympathetic plexuses; and (6) continuous irritation of the nervous plexuses of the pelvis by the invading tumor. Some of these factors cause disturbances in the physiology of pain receptors, lowering their threshold of excitation. In this way, even subliminal stimuli, usually painless, may elicite pain.

Anterolateral chordotomy was performed in 62 of the patients; in 22 of them the chordotomy was bilateral (carried out in 2 stages). In some patients the complications of chordotomy were considerable. Twenty-two patients experienced a slight paresis either in the ipsilateral leg or in both legs, which disappeared after 3 to 6 weeks (9 patients were already bedridden). Fourteen patients with unilateral and all with bilateral chordotomy complained for 3 to 6 weeks of impaired anal and bladder function, but in none were the sphincters permanently impaired. The results as regards relief from pain were satisfactory. Forty-one of the patients were still free from pain 12 months later. Five others were free from pain at the time they left the hospital, but no follow-up was possible. In 16 patients, the pain recurred 5 to 6 weeks later, either in the same side (10 cases) or in the opposite side (5 cases), but 14 of these responsed to intrathecal alcohol injection.

The intrathecal alcoholization of the posterior spinal nerve roots was also employed in the remaining 60 of the 122 patients who had been subjected to chordotomy. The procedure is as follows: One hour previous to the alcohol injection the patient is given a basic analgesic. Then 3 spinal puncture needles are successively inserted into the subarachnoid space between the spinal processes of the vertebrae L-3, L-4, L-5, and S-1. After checking the position of the needles, 0.5 to 1 cc. of alcohol is injected under slight pressure through each needle. The injection is instantly followed by a sensation of warmth or burning, giving place a few seconds later to a slight hypoesthesia in the cutaneous areas of the alcoholized posterior nerve roots and followed after 10 to 15 minutes by a complete analgesia. The intrathecal alcoholization is especially indicated in patients in a poor state of health, as well as in those who have become drug addicts and who could not stand the risks of a chordotomy, also in those who do not accept the operation. This method proved to be useful in patients with pain restricted to a few nerve roots and in patients complaining of residual pain after a chordotomy.

Late Results of Transplantation of the Tibial Tubercle in Recurrent Dislocation of the Patella. T. Jerre and B. Knutsson. Acta. orthop. scandinav. 27:141-152 (No. 2) 1957 (In English) [Copenhagen].

The authors accept Blumensaat's classification of dislocations of the patella, which differentiates the following groups: (1) recent dislocations; (2) recurrent dislocations, that is, dislocations occurring at intervals with the patella in proper position in the meantime; (3) constant dislocations. These are subdivided as follows: (*a*) habitual dislocations that occur every time the knee joint is flexed and (*b*) permanent dislocations in which the patella is always in a dislocated position. The paper is concerned only with those types of dislocations belonging to the Blumensaat group 2. Several surgical methods have been described for this form of recurrent patellar dislocation, but at the department of orthopedics in Hälsingborg transplantation of the tibial tubercle has been used during the last 20 years. This operation, which was recommended as early as 1888 by Lauenstein, is performed by the authors in the following way: A lateral lambdoid incision is made over the knee joint and extended a short distance proximal to the base of the patella and a few centimeters distal to the tibial tubercle. The ligamentum patellae is dissected, and the tibial tubercle is chiseled off. The ligamentous capsule of the knee on the outer side is slit longitudinally up to the level of the base of the patella. A thin bone flap is then chiseled up medially below the original site of the tibial tuberosity, and the tibial tuberosity is fixed under this bone flap, usually with a Rissler pin and a few absorbable (catgut) sutures, about 1 cm. medially and 1 cm. distally to its original site. After suturing the subcutaneous tissue and skin, the knee joint is fixed in a plaster cast with the knee flexed at about 10 degrees. The plaster is removed after 6 weeks, after which active and passive movements are begun.

This operation was performed on 32 joints in 28 patients, whose ages ranged from 15 to 45 years. There were no primary surgical complications. All

28 patients could be traced at the time of follow-up, from 1.1 to 19.7 years after operation. All except 1 patient, who was living abroad, could be reexamined. Eighteen patients stated that they had been free from symptoms since operation; 4 had had recurrences in the form of dislocations or subluxations. The region over the tibial tubercle was tender to palpation in 8 patients. In no instance was this sign severe, and on inquiry all 8 patients stated that this region only gave them a little trouble when they were kneeling on something hard. About one-third of the knee joints operated on showed a somewhat decreased range of flexion. Extension was not impaired in any. In general, symptoms were few and slight, but roentgenologic examination revealed arthrosis deformans in the knee joints of most of these patients. It is suggested that these changes might progress with time and might later cause symptoms in patients who are now free from them.

Technique and Results of Isolation of Cancer Cells from the Circulating Blood. S. Roberts, A. Watne, R. McGrath and others. A. M. A. Arch. Surg. 76:334-346 (March) 1958 [Chicago].

A physiological method for the isolation of cancer cells from blood utilizing differences in specific gravities is described. Step 1 of the procedure is the elimination of erythrocytes from whole blood, and step 2 is the separation of cancer cells from leukocytes. The erythrocytes are eliminated by the addition of fibrinogen, which causes rouleaux formation of erythrocytes and hence their accelerated sedimentation. The leukocytes and the tumor cells emain in the supernatant plasma in a homogenous uspension. This plasma suspension then is de- ted and layered, maintaining a sharp interface, r 5 cc. of isosmotic albumin solution which has een adjusted to a specific gravity of 1.065; this specific gravity is intermediate between that of most adenocarcinoma cells and leukocytes. After centrifugation most of the leukocytes, which are heavier than the adjusted albumin, will be packed in the bottom of the centrifuge tube, while most of the tumor cells, which are lighter than the adjusted albumin, will be collected at the plasma-albumin interface. The tumor cells are then aspirated from the albumin-plasma interface, resuspended in 10 cc. of isotonic sodium chloride solution, and centrifuged. This resuspension of the cells and recentrifugation remove albumin, which causes an undesirable red precipitate with the Papanicolaou stain. In order to improve the accuracy of differentiation of tumor cells and normal blood cells, the cancer cells isolated by this technique are compared with a direct smear of the tumor.

A total of 100 patients, 41 of whom had cancer of the digestive tract, 25 had cancer of the breast, 14 had cancer of the genitourinary tract, and 20 had miscellaneous cancers, and 14 control patients with nonmalignant diseases were studied by this technique. Blood samples were obtained from 1 or all of 3 venous sources: (1) peripheral blood samples from antecubital venipuncture; (2) aspiration of blood from a catheter inserted into the major venous trunk draining the tumor area; and (3) direct needle aspiration of blood from a vein draining the tumor site. Cancer cells were detected in the circulating blood from any or all of the 3 venous sources in 17% of patients who had been classified as curable and in 31% of those classified as incurable, indicating a direct relationship between the advancing stage of the malignant disease and the percentage of positive blood samples. Of 7 patients operated on, for whom adequate data before and during the surgical intervention were available for the evaluation of the role of the surgical manipulation, 6 showed an increase in the number of cancer cells in the circulating blood during manipulation incident to resection of the tumor. In 2 carefully studied patients, the cancer cells disappeared from the circulating blood within minutes after the removal of the primary carcinoma.

NEUROLOGY & PSYCHIATRY

Influence of Prior Active Immunization on the Presence of Poliomyelitis Virus in the Pharynx and Stools of Family Contacts of Patients with Paralytic Poliomyelitis. P. W. Wehrle, R. Reichert, O. Carbonaro and B. Portnoy. Pediatrics 21:353-361 (March) 1958 [Springfield, Ill.].

Sixty-seven persons, 12 being patients with paralytic poliomyelitis and 55 being family contacts of these patients, were studied by the authors in an attempt to obtain information regarding the degree of resistance to inapparent infection which may be conferred by immunization with formalized poliomyelitis vaccine, and to determine the influence of previous immunization on the quantity of poliomyelitis virus which can be detected in the pharynx and the feces. Isolation of poliomyelitis virus from the feces and from pharyngeal secretions of the immunized and nonimmunized household contacts of the patients with paralytic poliomyelitis showed that previous immunization does not prevent the acquisition of inapparent infection with poliomyelitis virus under conditions of household exposure. Although there was no apparent interference with enteric multiplication of poliomyelitis virus, an accurate estimate of the relative rates of acquisition of infection with poliomyelitis virus between immunized and nonimmunized children of comparable ages was not possible. However, enteric infection with poliomyelitis virus appeared to be slightly less frequently observed among the children household contacts in the age group from 5 to 9 years, toward which the immunization programs have been directed during the past 2 years, so that the members of this group were most frequently immunized. Poliomyelitis virus was present in the pharyngeal secretions of previously immunized contacts of patients with paralytic poliomyelitis less frequently and in lower titer during the study period than in those who had not previously received poliomyelitis vaccine.

Pharyngeal virus appears to be more sensitive to the presence of antibody than is enteric virus, and antibody is present in the pharyngeal secretions relatively early in the course of poliomyelitis infections. Thus, virus in this area might reasonably be expected to be neutralized more rapidly if the antibody-forming mechanisms were sensitized by previous immunization. Although there is no evidence that the air-borne route is important in the transmission of poliomyelitis, it seems reasonable to suspect that, in areas of good environmental sanitation and high standards of personal hygiene, contact transmission of pharyngeal virus may be important in maintaining this agent in the human population, particularly in view of the relatively high titers of virus observed in the pharynx. The authors' findings would suggest that this route may be rendered less effective after immunization.

An Analysis of Residual Disabilities (Paralysis and Crippling) Among 100,000 Poliomyelitis Patients: With Special Reference to the Rehabilitation of Postpoliomyelitis Patients. K. S. Landauer and G. Stickle. Arch. Phys. Med. 39:145-151 (March) 1958 [Chicago].

More than 300,000 persons alive today in the United States have had paralytic poliomyelitis, and more than 50% of them were attacked in the last decade. An estimated 90% of these recent poliomyelitis patients were reported by their physicians as severely, moderately, or slightly crippled at last notification. Of 102,184 patients hospitalized for poliomyelitis in the United States between 1952 and 1956, the cases of 64,146 with paralytic poliomyelitis were analyzed for residual disability or crippling in terms of the anatomic site or sites (most frequently multiple) affected. In addition, the records of 42,983 patients, aged 3 years and over, were analyzed for functional disabilities or, conversely, for remaining self-care capacity.

Of the 64,146 patients, 983 (1.5%) were totally paralyzed, 1,605 (2.5%) had severe paralysis of both arms and both legs, 3,749 (5.8%) had severe paralysis of both arms, and 9,900 (15.6%) had severe paralysis of both legs; 10,233 (16%) had some paralysis of 1 arm, 14,662 (22.9%) had some paralysis of both arms, 18,578 (29%) had some paralysis of 1 leg, 29,067 (45.3%) had some paralysis of both legs, and 9,600 (15%) had some degree of respiratory paralysis. At the time of discharge from the hospital, no residual disability (paralysis) was found in 10.2% of the 64,146 patients; there was slight disability in 22.4%, moderate disability in 41.1%, and severe disability in 26.3%. Functional disability at the time of discharge from the hospital was recorded as follows in the 42,983 patients: 13.6% were confined to bed, 6.7% were able to use the wheel chair only, 3.5% were able to stand only, 33% were able to walk with aids, and 43.2% were able to walk unaided. Self-care capacities among these 42,983 patients were recorded as follows: 24.4% of those confined to bed, 32.9% of those able to use the wheel chair only, 62.7% of those able to stand only, 81.7% of those able to walk with aids, and 92.6% of those able to walk unaided, were able still to feed, dress, and toilet themselves. Experience in 16 respiratory and rehabilitation centers shows that today's "hopeless" patients need not remain helpless, for through such integrated programs of research, care, teaching, and training comes the promise of help for even the most severely disabled.

Left Cerebral Hemispherectomy for Glioma in Infant Five Months Old. R. Cordero and F. Lichtenberg. Bol. Asoc. méd. Puerto Rico. 50:18-29 (Jan.) 1958 (In Spanish) [Santurce].

An infant, 5 months old, was hospitalized for the treatment of diarrhea and vomiting which had lasted 5 days. There was no fever. Moderate hydrocephalus and enlargement of the anterior fontanelle were observed. There were no neurological symptoms. Inasmuch as a subdural effusion or a chronic hematoma was suspected, repeated subdural puncture and examination of the cytochemical constituents of the spinal fluid were made. The quantity of fluid in the left subdural space was greater than in the right. After a few days of hospitalization and treatment, the digestive disorders disappeared. Hydrocephalus and enlargement of the anterior fontanelle, however, remained unchanged. Given a diagnosis of a subdural effusion or a chronic hematoma, the patient underwent a surgical exploration of the left hemicranial cavity 6 weeks after hospitalization. A cystic-nodular tumor which occupied almost all the left cerebral hemisphere was discovered and was removed by a left hemispherectomy. The patient stood the operation well; at the end, however, he stopped breathing and was pulseless for 20 minutes. He recuperated upon administration of oxygen, blood transfusion, intramuscular administration of neosynephrine, and the like. The tumor was pathologically classified as astrocytoma, grade 3. Samples of the tumor were sent to other pathologists. It was commented upon "as a most interesting combination of connective and glial tissue. One could hardly call it a neoplasm; it must be some sort of heterotopia of the nervous tissue. Tissue of this combination has been observed in superficial lesions of the cerebellum where the neuroepithelial tissue has not differentiated itself very well from the leptomeninx." The tumor has been provisionally designated as choristoglioma.

At the time of writing the patient is 18 months old. His head is slightly rotated to the left. He has facial paralysis on the right-central side, nystagmus with certain ocular movements, normal pupils, and right-sided spastic paralysis with conservation of voluntary movements of the legs. The Rossolimo sign is present in the right foot and moderately present in the left foot. Up to this age, the child has not spoken. The electroencephalographic records of the empty hemicranium show some electric activity. These records show a progressive tendency to normal stabilization. They also show asymmetrical waves of smaller voltage in the left side than in the right and epileptogenic tracings in the right side.

GYNECOLOGY & OBSTETRICS

Leukemia from Gynecologic Viewpoint. B. Fjällbrant. Nord. med. 59:177-179 (Jan. 30) 1958 (In Swedish) [Stockholm].

During the last 10 years 11 patients with leukemia were treated in the obstetric and gynecologic department in Lund and Malmö and the radiotherapy department in Malmö. From the gynecologic viewpoint leukemia is of greater importance than was formerly supposed. There are leukemoid infiltrations and ulcerations in the genital organs, and leukemia may cause menstrual disorders and abdominal pain. Only 1 patient was pregnant. Pregnancy rarely occurs in leukemia. No case of transission of leukemia to the infant has been reported. Most authors believe that pregnancy does not shorten the time of survival in acute or chronic leukemia.

Statistical Contribution to Problem of Etiology of Carcinoma of the Uterine Cervix: Its Incidence in Relation to Number of Births. K.-W. Franke and A. Eydam. Ztschr. Geburtsh. u. Gynäk. 149:297-323 (No. 3) 1958 (In German) [Stuttgart, Germany].

Whereas in some countries the death rate from cancer is now higher among men than among women, deaths from cancer in Germany were still more frequent among women than among men as late as 1950, the ratio being 42 to 36. This excess of cancer deaths in women is largely due to the frequency of carcinoma of the uterine cervix, which has remained high despite the efforts at cancer prophylaxis. The authors believe that a number of factors play a part in its development. Frequent deliveries and abortions have long been suspected as a contributing factor, and more recently endocrine factors have been suggested. The authors made statistical studies on the incidence of cervical carcinoma in relationship to the number of births at the women's clinic of the University of Erlangen, where 6,090 patients with cervical carcinoma were compared with 10,000 women with gynecologic disorders who were free from tumors. The average number of births for the patients with cervical carcinoma was 4.24, whereas for the control group of women it was 2.5. The authors, like other investigators, found that cervical carcinoma is most frequent in women between the ages of 45 and 55 years and that after the menopause the incidence of cervical carcinoma decreases noticeably. Patients with cervical carcinoma had a higher than average fertility. Carcinoma of the uterine cervix was considerably more frequent in women who had had several children than in women who were never pregnant. The authors conclude that, on the basis of their own observations and those of other investigators, the follicular hormone apparently plays a certain part in the pathogenesis of carcinoma of the uterine cervix, although other factors may appear to be even more important.

The Hazards of Elective Induction of Labor. W. C. Keettel, J. H. Randall and M. M. Donnelly. Am. J. Obst. & Gynec. 75:496-510 (March) 1958 [St. Louis].

The staff of the department of obstetrics and gynecology of the State University of Iowa Hospitals has had an extensive experience with the elective induction of labor at term. Obstetric patients come from all parts of the state, and when pregnancy is uncomplicated, they are brought to the hospital 2 weeks before term. The hospital facilities for such antepartum patients are limited. Because of the serious overcrowding, labor was induced in many of the indigent patients. Between 1926 and 1956, there were 28,253 patients delivered; labor was electively induced at term in 6,860 (24.3%) of this number. None of these patients had medical complications requiring induction, and all infants were alive and judged to be of term size at the time of induction. Each chart was reviewed, and the pertinent data placed on a standard punch card for ease of analysis.

Summarizing the results of this analysis of 6,860 electively induced labors, the authors state that the most effective method of inducing labor is simple amniotomy. Eighty-two and three-tenths per cent of the patients were in labor within 4 hours, and only 2.3% had a latent period of over 24 hours. Pitocin stimulation was used in patients with prolonged latent periods or desultory labors with intrapartum fever. Cesarean section must be considered when the latent period is prolonged and infection is present, if labor cannot be stimulated within 24 to 36 hours. There was 1 maternal death related to induction. The principal fetal hazards were prematurity, 3.1%; prolonged latent period, 5%; malpresentation, 0.9%; and prolapse of the cord, 0.3%. There were 6,889 babies born. Of these, 37 (or 0.6%) were stillborn, and 55 (or 0.8%) died during the neonatal period. The perinatal mortality was 1.4%. Thirty-nine of the perinatal deaths (0.6% of the babies delivered) were directly related to the elective induction. A conservative attitude should be maintained by the specialist toward the elective induction of labor. The average general physician should allow labor to start spontaneously.

Labor After Mitral Commissurotomy. G. Dellepiane. Minerva med. 49:1-3 (Jan. 6) 1958 (In Italian) [Turin, Italy].

Twenty-three women underwent mitral commissurotomy, 20 of them during pregnancy and 3 a few years (on an average 3 years) before pregnancy. Mitral commissurotomy was performed during the 3rd month of gestation in 7 patients, during the 4th month in 10, during the 5th month in 2, and during the 6th month in 1. Almost all the patients had a pleural reaction after the operation, in some instances accompanied by mild effusion, which subsided shortly. The uneventful postoperative course and freedom from recurrence of the rheumatic process were probably due to the protection afforded by cortisone which was related to gestation. From the obstetric point of view, labor was normal in 21 women. Two women had postoperative abortion. Anoxia related to the cardiovascular decompensation caused the intrauterine death of the fetus in 1 primipara during the third month of gestation. Circulatory decompensation in this patient had been corrected by the mitral commissurotomy. The abortion in the other, a multipara occurred during the 6th month of gestation and was probably unrelated to a cardiac disorder. This patient underwent the operation 3 years before pregnancy. Fourteen women had delivered up to the time of the writing of this report, while the others were still pregnant. The onset of delivery was spontaneous in all women. The delivery was carried out normally in 7, by the aid of forceps in 6, and by cesarean section due to obstetric condition in 1. Hemodynamic disequilibriums were not observed in any instance. Acute pulmonary edema developed in 1 woman at the beginning of the postpartum period. It was probably due to the failure of the previous surgical procedure to correct completely the mitral stenosis. Four women (30%) were allowed to breast-feed their infants.

The author recommends that women in whom mitral stenosis is discovered during pregnancy should have the operation performed during pregnancy unless it is specifically contraindicated. This opinion is based on 2 facts: 1. There is a mortality of 7 to 10% during the puerperium in women in whom mitral stenosis has not been corrected by commissurotomy. 2. There have been no postoperative complications attributable to mitral commissurotomy.

Caesarean Section at the Winnipeg General Hospital Maternity Pavilion, 1951-1956. C. R. Bradford. Canad. M. A. J. 78:392-397 (March 15) 1958 [Toronto].

The data presented here were taken from the records of the maternity pavilion of the Winnipeg General Hospital from Jan. 1, 1951, to Jan. 1, 1956. Procedures included as cesarean sections were those performed on a patient from the 28th week of pregnancy onward or those in which the fetus weighed more than 500 Gm. (1¼ lb.). There was a total of 19,379 deliveries. Of this number, 476 were by cesarean section. This is an incidence of 2.45%. In 1951 the incidence was 2%, and since that time there has been a gradual increase to 2.8% in 1955. There were no maternal deaths due to, or associated with, cesarean sections. During the same period of time there were 7 maternal deaths among 18,903 vaginal deliveries, an incidence of 3.7 per 10,000. On examination of the records of the 7 patients, it was found that in no case would a cesarean section have influenced the final outcome.

The use of the classical method of cesarean section has been decreasing in most obstetric hospitals, and this has also been the case in Winnipeg. However, of the 476 sections studied, 85 (or 18%) were of the classical type. This rate is regarded as too high, but 62 of these were done by physicians and surgeons who did not limit their practice to obstetrics and gynecology. The indications for cesarean section accepted at the Winnipeg hospital are those formulated by Bryant in 1950, the major ones being (1) mechanical obstruction to delivery, (2) bleeding, and (3) hypertensive disease. There were 295 primary cesarean sections, 177 repeat sections, and 4 sections after previous hysterotomy. For primary sections, more than 1 indication was often given. Sections in which there were obstetric or medical complications that would probably influence the immediate outcome for mother or baby were considered as emergency procedures. There were 174 emergency and 302 elective sections. Almost all the repeat sections were elective. Thirteen patients had elective section for disproportion, and 13 elderly primigravidas had elective primary section without trial of labor.

When the maternity pavilion first opened, ether-chloroform mixture was used as the anesthetic for most vaginal deliveries and procaine spinal for most cesarean sections. Now cyclopropane, nitrous oxide, and oxygen are used for most vaginal deliveries, and this combination, plus thiopental (Pentothal) and relaxing agents, is used in the majority of cesarean sections. Tubal ligation was carried out at the time of cesarean section in 20% of the women. All except 4 of those sterilized were multiparous. There were 479 babies delivered, including 3 sets of twins. Seventy-three (15%) weighed under 2,500 Gm. (5½ lb.) and were considered premature. Among the elective sections there were 16 (3.3%) premature babies, and of this group 3 died. Of the 479 babies, 6 (1.4%) were stillborn, and 25 (5.2%) died in the neonatal period. This resulted in a gross fetal loss of 6.4%. Among the neonatal deaths in all cesarean sections in this series, prematurity was the biggest problem. In this connection it is suggested that perhaps the maternal risk would not be too much increased if more women were allowed to commence labor before elective section was performed.

Studies in Prolonged Pregnancy: Part IV—Clinical Assessment. C. H. G. Macafee and G. Bancroft-Livingston. J. Obst. & Gynaec. Brit. Emp. 65:7-15 (Feb.) 1958 [London].

Of 1,852 pregnant women who were admitted for delivery to the Royal Maternity Hospital, Belfast, between 1956 and 1957, 386 (21%) had pregnancies prolonged beyond 287 days, and 143 (7.7%) had pregnancies which exceeded 294 days. Among the 1,852 deliveries there were 81 stillbirths, an incidence of 4.4%. Among the deliveries of women whose pregnancies exceeded 287 days, there were 10 stillbirths, and among those of the 143 women whose pregnancies exceeded 294 days, there occurred 6 stillbirths (4.2%). There was one congenital abnormality (gross cardiac defect) incompatible with life, giving a corrected figure of 3.5%. Five neonatal deaths occurred after pregnancies lasting more than 294 days; in 4 of these 5 cases the fetus was abnormal, and in the 5th birth trauma seemed likely because of the difficulty encountered in the delivery of the infant weighing 4762.7 Gm. (10½ lb.). This incidence of stillbirths and neonatal deaths compared favorably with that previously reported, despite the fact that routine induction of labor did not figure in the treatment. Routine induction of labor 5 to 7 days after the calculated date is to be considered as meddlesome midwifery. Forceps delivery was indicated in 32% of the women whose pregnancies exceeded 294 days, as compared with the over-all hospital forceps rate of 15.6%. The cesarean section rate of 6% among the women with prolonged pregnancy was not higher than the over-all figure for the hospital. Thirty-three (23%) of the women in this group had a labor which lasted more than 24 hours, and in 18 of these meconium was present for varying periods of time. As the average duration of labor for primigravid women in the hospital is 16.9 hours, prolongation up to or beyond 24 hours is significant.

These data would suggest that mechanical difficulty plays an important part in prolonged pregnancy; the role of hypoxia in prolonged pregnancy, however, has been overemphasized. The significance of the presence of meconium at artificial rupture of membranes or during labor has been erroneously interpreted as resulting from fetal hypoxia due to placental insufficiency. Meconium as the result of hypoxia may be due to compression of the cord either as the result of prolapse or extreme shortening, not primarily to placental insufficiency. The presence of meconium during labor may indicate an earlier episode of fetal hypoxia, but if the fetal heart is undisturbed, one may adopt a conservative line of treatment. When meconium appears in a prolonged labor, cephalopelvic disproportion which may interfere with placental function must be excluded, as cesarean section may be the correct method of treatment. In the absence of disproportion it is only the occasional case which will give rise to anxiety, but careful observation of the fetal heart is essential, and, if necessary, a forceps delivery to shorten the second stage. The above advice is applicable regardless of the maturity.

PEDIATRICS

Some Common Medical Problems Encountered in Mentally Retarded Children. C. Drayer and I. Mauss. New York J. Med. 58:670-674 (March 1) 1958 [New York].

Fifty retarded children, between the ages of less than 1 year and 16 years, were selected at random and studied regarding causation of mental retardation, nutritional status, susceptibility or unusual reactions to illness, congenital abnormalities, abnormal neurological findings, and accident proneness. Of the 50 children, 39 were not of the type with mongolism and 11 were of the type with mongolism. Seven (14%) of the 50 children had a birth weight of less than 2494.75 Gm. (5½ lb.), as compared with the normal incidence of 5 to 10%. Nine of the 11 mothers of children with mongolism were over 30 years of age at the time of delivery, confirming the frequent observation that mothers of children with mongolism are older at time of delivery than mothers of normal children. Developmental or embryologic causative factors of retardation were found in 10 children; birth trauma was considered a causative factor in 7, postnatal encephalitis in 4, a skull fracture sustained at the age of 1 year in 1, and a hereditary factor (lipochondrodystrophy) in 1. Causative factors were not determined in the remaining children.

There did not seem to be any significant deviation from the normal nutritional status. The number of children (25) with head circumferences well below normal was far out of proportion to what one would find in the general population. Only 3 children showed an unusual tendency to the occurrence of high fever, in contrast to the common belief that retarded children are prone to high fever. Twelve children either had a convulsive disorder or gave a history of convulsions. The convulsive episodes were followed by retardation in 2 of these. None of the children with mongolism had convulsions. Among the congenital abnormalities, strabismus was found in 16, congenital heart disease in 3, and extreme arching of the palate in 18. Twelve children (25%) showed no evidence of any congenital abnormalities. The incidence of congenital abnormalities in the 50 retarded children, however, seems higher than one would expect to find in the general population. Only 2 children showed a tendency to fall, but even these 2 did not sustain severe injuries in their falls. Twenty-seven children showed one or more abnormal neurological findings, such as abnormal gait, poor coordination, spasticity, athetosis, abnormal reflexes, and intention tremor. The authors are convinced that with proper management, appropriate group experiences, education up to capacity, and the aid of sheltered workshops more satisfactory adjustments can be made by many of the more severely retarded children.

Malignant Abdominal Tumors: Present Condition of Three Little Girls Three Years After Operation. L. Gubern Salisachs. Rev. españ. pediat. 14:39-46 (Jan.-Feb.) 1958 (In Spanish) [Saragossa].

Abdominal cancer in children is more frequent than is believed. It is curable, provided that the patient is observed within the period of operability of the tumor. The 2 most frequent types of malignant abdominal tumors in children are Wilms's tumor and sympathoblastoma. The subjects of this report are 3 girls, aged 4 years, 3 years, and 1 year respectively. The first patient had lost weight for 2 months before observation. An abdominal tumor was found by palpation. It grew rapidly to the size of the head of a fetus. Roentgenologically it appeared to be a renal tumor. Preoperative roentgenotherapy consisted of 10 sessions of 200 r each. This treatment was followed by 4 days of rest, after which a nephrectomy was performed. Biopsy showed a Wilms tumor. Postoperative roentgenotherapy consisted of 10 sessions of 200 r each. The second patient had an abdominal tumor which had grown rapidly for 4 months before observation. Clinical and roentgenologic examination showed a left-sided renal tumor. Nephrectomy on the left kidney was performed. Biopsy showed a Wilms tumor. Postoperative roentgenotherapy was given up to a total dose of 4,000 r. The third patient had abdominal colic and vomiting for 2 days before the observation. An abdominal tumor in the umbilical region was found by palpation. It seemed to be attached to the neighboring structures. A paravertebral tumor attached to the pancreas, the vena cava, the portal veins, and the choledochus was found and removed. A cholecystogastrostomy was performed 2 weeks after the operation to relieve obstructive jaundice. Biopsy showed the tumor to be a sympathoblastoma. Postoperative roentgenotherapy was started on the second day after the first operation. It was continued to reach a total dose of 2,500 r.

The 3 patients are apparently clinically cured at periods of more than 3 years and nearly 4 years. The biological time of cure of cancer in children without any recurrences for more than a year corresponds to that in adults of more than 5 years after the operation. The author emphasizes the need of not palpating the abdomen of children with symptoms suggestive of abdominal cancer. Abdominal tumors should be considered in the group of acute diseases of the abdomen. The abdomen should not be touched. In American hospitals as soon as children with acute abdominal disease suggesting an abdominal cancer are admitted, the patients are tagged with a note saying: "Please don't feel my tummy." By this means, dissemination of cancer cells is prevented.

Primary Hypophosphatemic Familial Vitamin-Resistant Rickets. M. Lamy, P. Royer, J. Frezal and H. Lestradet. Arch. franç. pédiat. 15:1-24 (No. 1) 1958 (In French) [Paris].

Observation of 3 patients with hypophosphatemic vitamin-resistant rickets prompted this study of the disease, which is hereditary and apparently familial in two-thirds of the reported cases. Two of the authors' cases appeared as phosphatic diabetes, which was transmitted as a dominant characteristic affecting various members of the two families in several generations; the third, which appeared as a renal aminophosphatic diabetes, was isolated and could not be proved to be familial. Severe clinical anomalies appear in one-third of the children of affected persons; consequently, since the disease usually begins in the 2nd year of life, the children of affected parents should be kept under observation from the age of 1 year on, so that treatment can be given, if needed, before dwarfism and severe skeletal deformities have time to become established.

The principal clinical signs of this form of rickets are functional disturbances, dwarfism, and skeletal deformities. Fatigability is often pronounced; osseous pains are not uncommon; and walking is delayed for several months. The muscular tone, on the other hand, is good, in contradistinction to the hypotony of ordinary avitaminic rickets. Another difference is the lack of hypocalcemic tetanic complications in primary hypophosphatemic vitamin-resistant rickets. The dwarfism, which becomes more and more apparent as the child grows, is characterized by micromelia, especially of the legs. The osseous deformities are seen chiefly in the legs and in the spine, but they may appear elsewhere, e. g., in an olympic brow and in enlargement of the bridge of the nose. The roentgenologic signs closely resemble those of ordinary avitaminic rickets.

The biochemical signs are to be sought in the urine, the blood, and the feces. Calciuria is minimal, and the Sulkowitch reaction is either negative or weakly positive; phosphaturia is abundant, but albuminuria, melituria, and hyperaminoaciduria are lacking, and this distinguishes the condition from ordinary rickets and from the de Toni-Debré-Fanconi syndrome. Finally, the urinary sediment is normal. Analysis of the blood serum shows that the calcium level is normal or occasionally slightly lowered; phosphatemia is always low, between 10 and 30 mg. per liter; and the alkaline phosphatase is moderately elevated, usually standing between 15 and 25 Bodansky units. This level declines fairly rapidly, becoming normal again between the ages of 10 and 18. A defect in calcium absorption is revealed by examination of the stools. Renal function is generally normal, but the renal clearance of phosphates is high, as might be expected from the coexistence of hyperphosphaturia and hypophosphatemia, and the coefficient of tubular reabsorption of filtered phosphate is lowered, as demonstrated in one of the authors' patients, in whom it was 82% instead of the normal 92 to 95%. The response obtained to the intravenous perfusion of calcium gluconate (Howard test) in one of the patients led the authors to believe that the renal phosphatic diabetes in this patient was secondary and that the primary defect is prerenal. The disease pursues a chronic course. It continues to be active until the patient reaches the age of 15 to 20 years, when it enters a period of latency during which, although the patient remains dwarfed and presents multiple skeletal deformities, the subjective symptoms disappear, the roentgenologic anomalies are lessened, and the biochemical disorders are repaired, except for the hypophosphatemia. Relapses may occur during pregnancy or lactation.

Several theories have been advanced to account for hypophosphatemic familial vitamin-resistant rickets. It would apparently be premature to choose between them at the present time, but certain partial conclusions seem to be warranted. The primary factor is probably a defect in the intestinal absorption of calcium linked, not to a general insensitivity to vitamin D, but to the mechanism of calcium absorption, which does not depend on this vitamin. The second factor is hyperparathyroidism as in ordinary rickets; this is responsible for the increase in the renal clearance of phosphate and perhaps for the different anatomic aspects of the osseous lesions. Presumably, then, vitamin D in large doses acts by bringing about a discreet increase in the digestive absorption of calcium, perhaps by mobilizing calcium from the bones and, finally, by direct blocking of the parathyroids.

Treatment consists of vitamin D administration and osteotomy. Vitamin D (D_2 or D_3) should be administered uninterruptedly in large doses, adjusted to produce the highest phosphatemia possible without exceeding 111 mg. per liter of calcemia, or 400 mg. per 24 hours of calciuria. The object should be to find the dose that is effective without being toxic, and the child's parents should be instructed in regard to the signs of vitamin D intoxication, which is always to be feared. The primary purpose of osteotomy is to correct deformities of the lower limbs. The immobilization osteoporosis to which it leads has a definitely beneficial effect on growth in stature, on the diaphysial and epiphysial roentgenologic signs, and on the biochemical signs, producing, among other things, an abrupt drop in the alkaline phosphatase level. To prevent vitamin D intoxication, administration of the vitamin should be discontinued before and for some time after osteotomy. Continuance of the treatment during the adult period depends on the patient's tolerance for the disease; in most cases, however, it should be discontinued at this time.

Evaluation of Success of the Dietary Treatment with Casein Hydrolysate Poor in Phenylalanine for Oligophrenia Phenylpyruvica. R. Grüttner, F. Müller and H. Wallis. Monatsschr. Kinderh. **106**:41-45 (Feb.) 1958 (In German) [Berlin].

The authors report on 2 boys, aged 2 years and 3 months and 3 years and 3 months, respectively, and 1 girl, aged 1 year and 3 months, with oligophrenia phenylpyruvica, in whom determinations of the phenylpyruvic acid excreted in the urine were carried out and who were placed on a diet in which a casein hydrolysate to which tyrosine and tryptophan had been added was used as a protein source. The children received daily 2 to 2.5 Gm. of this hydrolysate per kilogram of body weight. Fat was given in the form of coconut margarine and olive oil (daily amount of 3 Gm. per kilogram of body weight), and carbohydrates in the form of grape sugar and wheat starch (daily amount of 10 Gm. per kilogram of body weight). Vitamin compound preparations and fruit juices also were given.

After 6 weeks' treatment with this diet, the excretion of phenylpyruvic acid in the urine was reduced from 187 mg. per 100 cc. to about 20 mg. per 100 cc. in the 2 younger children, i. e., the excretion of the phenylpyruvic acid was restored to normal. Control of the disturbance of metabolism thus was obtained in these 2 patients. In the 3-year-old boy, the excretion ~~of the~~ phenylpyruvic acid in the urine was considerably reduced but was not restored to normal; the "lightening and nodding" cramps, however, subsided. Much emphasis has been put on the development of static and mental functions as an aid in the evaluation of the dietary therapy. A certain improvement in these functions was obtained in all 3 children, but the backwardness of the children remained so pronounced that severe idiocy was considered to be the right term for their condition. In the girl, a protein deficiency syndrome occurred after 3 months of the dietary treatment, manifested by edema and reduction of the serum protein level to 3.2 Gm. per 100 cc.; apparently mobilization of the autogenous protein resulted, which caused an increase in the pathological decomposition products of phenylamino-propionic acid (phenylalanine) and, therefore, an increased excretion of phenylpyruvic acid. The risk of such a complication has been stressed.

The authors agree with Armstrong and other workers that success of treatment with a diet poor in phenylamino-propionic acid may be expected only in children who are placed on this diet during the first months of life and in whom this treatment is continued throughout life. Irreparable damage of the substance of the brain must be taken into account when this therapy is instituted in the second or the third year of life; normalization of the mental functions than has become impossible.

The Gastro-Oesophageal Region in Infants: Observations on the Anatomy, with Special Reference to the Closing Mechanism and Partial Thoracic Stomach. G. S. M. Botha. Arch. Dis. Childhood 33:78-94 (Feb.) 1958 [London].

The nature of the closing mechanism between the esophagus and the stomach has been studied chiefly in adults; the anatomy in the infant, which does not necessarily correspond, has not received the same attention. The diaphragm, lower esophagus, upper stomach, aorta, and surrounding tissue were removed en bloc from 115 infants. Every specimen was dissected, and drawings were made of the essential features. In age, the subjects varied from a 32-week-old fetus to an 8-year-old child. In the great majority the ages ranged from a few hours to 1 month. One fetus weighing 520 Gm. (1 lb. 2 oz.) and 1 girl of 13 years were also studied. The sexes were about equally represented. In addition to the dissected specimens, numerous studies were carried out in the autopsy room where the organs were examined in situ. Unlike in the adult, the hiatus in the infant was found to be of uniform size. It was small, so small that the narrowest portion of the esophagus could just pass through. The esophagus was gripped firmly. The outstanding features of the gastroesophageal region in infants and children were a small powerful hiatus with marked overlap and an oblique lengthy tunnel, a formidable phrenoesophageal membrane, and secure fixation of a narrow terminal esophagus. These features were considered to be mainly responsible for the superior gastroesophageal competence in infancy.

Since competence of the cardia and fixation of the esophagus are proportionately much better in the infant than in the adult, a partial thoracic stomach which causes vomiting immediately after birth is not merely a "slight herniation" but a major derangement. The author cites evidence to the effect that a partial thoracic stomach in infancy is a congenital abnormality in the great majority of cases. Differences in age, sex and familial incidence, clinical course, roentgenologic features, associated abnormalities, and outcome of surgery support the view that the mechanism of partial thoracic stomach in infancy and hiatus hernia in adults are not identical conditions. The noncommittal term "partial thoracic stomach" is preferred, as it is impossible in the great majority of cases to distinguish between sliding hiatus hernia and congenital short esophagus. The author concludes that evidence suggests that a large proportion of cases of partial thoracic stomach are due to congenital short esophagus, whereas, in contrast, hiatus hernia in the elderly is a degenerative manifestation in the evolution of the cardiac region.

Congenital Multiple Arthrogryposis. R. Joseph, D. Pellerin and J. C. Job. Semaine hôp. Paris. 34:525-536 (Feb. 24) 1958 (In French) [Paris].

Congenital multiple arthrogryposis is characterized by stiffness of the joints of the limbs, by paralysis with amyotrophies, and by muscular retractions. There may be associated malformations, some of which seem to depend on the muscular involvements. The condition is congenital and not progressive. On the contrary, the deformities present at birth sometimes become attenuated under the influence of mobilization. A brief review of the literature shows that before and after Stern, in 1923, introduced the now widely used, although not quite suitable, term "congenital multiple arthrogryposis," the condition was described under other terms. It is really a neuromuscular disease, and the authors feel that the following terms are the most suitable ones: "multiple congenital contractures," "congenital amyoplasia," and "deforming fetal myodystrophy." The causes of the condition are still unknown. The genetic origin often suggested does not fit all the facts. The hypothesis that it is an acquired embryopathy has not been fully confirmed. The authors believe that infants with the disorder recently observed by them illustrate the etiological problem.

One child was born after a normal pregnancy into a family without consanguinity or genetic anomalies. During the third month of gestation the mother had had daily contact with a child who was a carrier of poliomyelitis virus. However, at the time of delivery the virus was absent from mother and child, and the significant level of neutralizing antibodies did not show whether poliomyelitis had been transmitted to the mother during pregnancy. Two infants in a family of 4 children had typical congenital multiple arthrogryposis. There was no consanguinity in the parents, and the family history revealed no anomalies comparable to multiple arthrogryposis. Biopsy of muscular tissue revealed fibers with degenerative lesions interspersed between normal fibers. A fourth child with arthrogryposis had 4 normal siblings, and again there was no consanguinity. In this child some of the muscles of the trunk also showed aplasia or paralysis.

The disorder is not extremely rare, over 250 cases having been reported. Pathological studies prove that the osteoarticular deformities are secondary to the atrophies. The latter are neurogenic. In 10 of 11 cases with complete anatomic studies, the muscular atrophy was accompanied by rarefaction or degeneration of the motor neurons of the spinal cord. The possible relationship of congenital multiple arthrogryposis to other congenital neuromuscular disorders is discussed. A disturbance acting on the motor neurons of the fetus before the 4th month of gestation is accepted as the pathogenetic mechanism of this disorder.

DERMATOLOGY

Morbidity Incidence of Certain Types of Dermatosis in 1946 and in 1956 at Istituto Dermopatico dell' Immacolata at Rome. R. Cavalieri. Cronache Ist. Dermopat. Immac. 12:205-208 (Nov.-Dec.) 1957 (In Italian) [Rome].

Statistical data about persons with various types of dermatosis who received treatment at the outpatient department of the Istituto Dermopatico dell' Imacolata in Rome in 1946 and 1956, were compiled and assessed. Patients with common skin disorders were not included in this series. The disorders in decreasing order of severity were as follows: psoriasis, alopecia, varicose ulcer, trichophytosis, urticaria, herpes zoster, herpes simplex, vitiligo, epithelioma, lichen, erythema multiforme, and others. In 1946, 11,467 diagnoses and in 1956, 23,987 diagnoses were made. Morbidity incidence increased in 1956, as compared with 1946, for alopecia, epithelioma, erythema multiforme, herpes, lichen, psoriasis, and vitiligo. This statistical assessment probably reflects the present conditions. Decrease in the same period was noted for acariasis, erythema, leishmaniasis, lupus vulgaris, urticaria, dandruff, trichophytosis, and varicose ulcer. Statistical evaluation is probably accurate for the types of dermatosis which are caused by parasites. This improvement can be ascribed to hygienic and prophylactic measures introduced during the last 10 years. Decrease in the incidence of lupus vulgaris is largely due to the advent of antibiotics and of vitamin D_2. Decrease in the incidence of leishmaniasis at this institute does not correspond with actual conditions for the whole country. Reports from other areas where leishmaniasis is endemic in Italy still show a high incidence of the disease.

The Prophylactic Treatment of Poison Ivy Dermatitis with 3-n-Pentadecyl Catechol Using the Wheal Method. H. Keil. New York J. Med. 58:57-59 (Jan. 15) 1958 [New York].

This communication records the results of making wheals in the skin with small doses of synthetic 3-n-pentadecyl catechol in the prophylaxis of poison ivy dermatitis. So far as the author knows, this is the first attempt to use this method to influence directly the "shock organ" (probably the basal layer in the epidermis) in this type of allergic contact dermatitis. This procedure was carried out in 28 patients who received in all 38 full courses of prophylactic treatment, each course consisting of 6 consecutive wheals made at weekly intervals. The optimal dose for the production of wheals was 0.2 cc. of 0.001% solution of synthetic 3-n-pentadecyl catechol in sterilized peanut oil. By placing the solution very close to the "shock organ" of the skin, an attempt was made to cause 6 mild attacks of localized and controlled poison ivy dermatitis. The clinical results observed with this form of treatment were as follows: Twenty courses were followed by complete freedom from attacks of poison ivy dermatitis; 16 courses were followed by transient abortive attacks; and 2 courses were regarded as failures. The clinical evidence, aside from the 2 failures, supports the view that the wheal method of prophylaxis with synthetic 3-n-pentadecyl catechol produces clinical hyposensitization. It is also probable that this hyposensitization lasts generally, but not always, for about 3 to 4 months after the treatment.

OPHTHALMOLOGY

Does Electric Convulsive Therapy Cause Cataract? M. Koskenoja and C. C. Runeberg. Acta ophth. 36:102-109 (No. 1) 1958 (In English) [Copenhagen].

Since the introduction of electric (convulsive) shock therapy it has been suggested by some investigators that the therapy may either produce an electric cataract or accelerate the development of senile cataract. At the outpatient department of the University Eye Clinic of Helsinki, the authors observed a patient who complained of marked impairment of visual acuity after electric shock therapy. He had a bilateral cataract of a type suggestive of an electric cataract. Therefore, the authors were prompted to investigate whether an electric cataract is a complication after electric shock therapy, although in the case of this patient it was later demonstrated that electric therapy was not the cause of his cataracts. Studies were made on the eyes of 633 patients in a mental hospital. Nine persons with typical congenital cataract were excluded. Electric shock therapy had been given to 237 of the patients, whereas 396 patients had not received such treatment. The statistical analysis of the findings did not demonstrate that electric shock therapy produces electric cataract.

Investigation into the Control of Trachoma in Sekhukuniland. J. A. Pratt-Johnson and J. H. W. Wessels. South African M. J. 32:212-215 (Feb. 22) 1958 [Cape Town].

These studies were made in a native reserve in the northeastern Transvaal, with a population of 160,000 belonging to the Bapedi Bantu tribes. It was found that 100% of the population living on the "flats" had trachoma, but the inhabitants of the plateau or the neighboring mountains were free from the disease. Investigations suggested that the incidence of trachoma in this population depends on 2 factors: the prevalence of swarms of flies, which directly convey the infection, and the acute shortage of water, which prevents minimal hygienic precautions. Both of these factors exist on the "flats." Where the mountain dwellers live, on the other hand, there is no lack of water and only a few flies are found. Two important points were recognized during the treatment of trachoma: 1. Sulfonamides given parenterally and antibiotic ointment used locally arrest active trachoma and rapidly clear all evidence of the commonly associated secondary infection. 2. The hospital records show that this treatment is futile, because many children are treated as many as 4 times during the summer for subacute mucopurulent conjunctivitis. The authors doubt that a strain resistant to this therapy has developed, and they are unable to ascertain whether reinfection by flies includes the trachoma virus, or whether it is confined to commonly associated organisms, such as the Koch-Weeks bacillus. It appears that most emphasis should be laid on the prevention of trachoma by an attack on the fly plague and the provision of an adequate water supply.

OTOLARYNGOLOGY

Premedication in Clinical Audiometry: An Investigation of the Effect of Mephenesin Carbamate (Tolseram) on Normal Hearing Thresholds as Determined by the Conditioned Psychogalvanic Skin Response and Conventional Pure-Tone Audiometry. R. B. Strauss. A. M. A. Arch. Otolaryng. 67:354-363 (March) 1958 [Chicago].

Twenty-four men, between the ages of 21 and 28 years, with normal hearing, were tested in 4 ways by means of a Latin-square counterbalanced order. Each person's hearing thresholds at 500 cycles per second (cps), 1,000 cps, 2,000 cps, 4,000 cps, and 8,000 cps were estimated by conventional pure-tone audiometry after the administration of mephenesin carbamate or a lactose placebo, as well as by psychogalvanic skin-response audiometry after the administration of mephenesin carbamate or a suitable placebo. To indicate hearing acuity, the psychogalvanic skin-response audiometric method uses changes in skin resistance in response to a pure tone (conditioned stimulus) which occur after the skin resistance of the person, whose hearing acuity is tested, has been conditioned by a slight electric shock (unconditioned stimulus). A statistical analysis of variance of the quantitative data indicated that mephenesin carbamate in the dosage used had no statistically significant effect on hearing thresholds as determined by either psychogalvanic skin response or conventional pure-tone audiometry. Furthermore, no significant differences between hearing thresholds of the same persons were found, whether measured by conventional pure-tone finger-raising technique or by psychogalvanic skin-response audiometry.

The rationale for this study stems from the inadequateness and unreliability of conventional means of testing the hearing of infants, children, malingerers, and persons with psychogenic deafness. Normally active young children and hyperactive patients with neuromotor disorders cannot be tested satisfactorily by psychogalvanic skin-response audiometry either, because their activity interferes with the correct interpretation of the galvanic responses. Since mephenesin carbamate, an orally effective, centrally acting, skeletal muscle relaxant, may be used without interfering with or significantly affecting hearing thresholds, a way is paved for further inquiry as to the effectiveness of the drug in reducing the activity of normal children and the hyperactivity of patients with neuromotor disorders, so that this drug may be utilized as premedication to facilitate hearing testing.

THERAPEUTICS

Long-Term Treatment of Angina Pectoris with Dicumarol. Z. Gabrielsen and J. R. Myhre. Circulation 17:348-353 (March) 1958 [New York].

An attempt was made to register by use of "report cards" the daily amount of anginal pain and the weekly consumption of glyceryl trinitrate (nitroglycerin) tablets in 9 men and 1 woman, between the ages of 42 and 61 years, with normal blood pressure and with arteriosclerotic heart disease and angina pectoris, during treatment by alternating courses of bishydroxycoumarin (Dicumarol) tablets and placebo tablets. Acute myocardial infarction had occurred previously in 4 of the 10 patients. All the patients had had their symptoms for at least 1 year, and 4 patients had had symptoms for more than 3 years. One died shortly after the initiation of the study, and only 6 managed to keep count of their glyceryl trinitrate consumption. The total number of bishydroxycoumarin courses was 24, 12 of them lasting more than 6 months during a total period of 2 years of observation. Graphic records of the values for pain, as calculated from the daily report cards, and of the values for the consumption of glyceryl trinitrate tablets did not indicate that treatment with bishydroxycoumarin had a greater effect than treatment with placebos on the cardiac pain in the patients with angina pectoris of more than 1 year's duration.

Fibrinolytic Treatment of Thrombo-Embolic Diseases with *Purified Bacterial* Pyrogens. P. Meneghini. Acta haemat. 19:65-81 (Feb.) 1958 (In English) [Basel, Switzerland].

In an attempt to study the value of activating fibrinolysis by means of highly purified bacterial lipopolysaccharides, 58 patients with thromboembolic disease were given a proprietary preparation of a highly purified lipopolysaccharide derived from Salmonella abortus equi (Pyrexal) or a proprietary preparation of acetylated lipopolysaccharide derived from Escherichia coli. Thirty-eight of the patients had thrombophlebitis, which was complicated by pulmonary embolism in 5, 9 had peripheral arteritis, and 11 had postphlebitic syndrome. The patients received an initial intravenous injection of 0.2 mcg. of Pyrexal; for this purpose, the 2-cc. ampul containing 1 mcg. of the drug was diluted with 8 cc. of isotonic sodium chloride solution, and then 2 cc. of this dilution was injected. More recently, ampuls of 5 cc. containing 0.5 mcg. became available, from which small initial doses of 0.2 mcg. were readily withdrawn. Treatment with the second lipopolysaccharide preparation was started with a dose of 50 mcg. given intravenously (dilution of the the 2-cc. ampul containing 200 mcg. with 8 cc. of isotonic sodium chloride solution, and injection of 2.5 cc. of this dilution). Depending on the reaction of the individual patient, the dose of Pyrexal was increased by 0.1 to 0.2 mcg. per injection, and the dose of the other preparation was increased by about 40 mcg.; the required febrile reaction was thus obtained almost without exception. The pyrogen injections were generally given at intervals of 2 days to let the patient recover sufficiently from the shock. The injections were given every other day when the patient was not significantly affected by the fever therapy.

Treatment with the tested preparations had the advantage over that with vaccines and that for a similar fibrinolytic activity in that the febrile period was shorter and lasted only about 6 to 8 hours and that the undesirable side-effects were less pronounced. The rise of temperature occurred within about 1 hour after the injection; temperatures of 38 C (100.4 F) to 39 C (102.2 F) were often associated with intense rigor lasting for 1 hour. When the patient was given effective antipyretic premedication, the temperature rose only to 37.5 C (100 F). The therapeutic results were as satisfactory as those obtained with vaccines, which were reported on previously. In the patients with arteritis, the bacterial polysaccharides acted chiefly on the thrombosis, by which the arteritis was complicated, and promoted the establishment of an effective collateral circulation. Pyrogen-induced fibrinolysis brought about a suprisingly quick recovery both in patients with phlebothrombosis and thrombophlebitis and in patients in whom embolic complications had already occurred. The febrile reaction can be mitigated with the aid of antipyretic medication (especially sodium salicylate), which does not interfere with the activation of fibrinolysis. Combined therapy with anticoagulants and fibrinolysis elicited by bacterial lipopolysaccharides is advisable, since blood clotting and fibrinolysis are controlled by 2 different enzyme systems. Anticoagulants are valuable chiefly because of their preventive effect on thrombosis and its spread. The response to artificial fever therapy is so rapid that one can hardly question the thrombolytic process involved in the activation of fibrinolysis which results from this measure.

First Experiences with the Use of Meprobamate in the Therapy of Cardiovascular Disorders. F. Fontanini and A. Rivi. Minerva med. 48:4499-4503 (Dec. 26) 1957 (In Italian) [Turin, Italy].

Usefulness of meprobamate as a psychotherapeutic agent has led the authors to administer it to 52 patients who have had cardiovascular disorders associated with psychoneurotic anxiety and tension state. Patients were divided into 3 groups. The first group was composed of 12 patients with functional cardiac disorders, the second of 21 patients with organic heart disease, and the third of 19 patients who had various types of hypertension associated or not with heart disease. The daily dosage was 500 mg. given in 1 or 2 tablets. The first group received meprobamate alone, whereas the others received the drug as an adjunct to the basic therapy, but with the exclusion of any other sedative.

Meprobamate produced partial or complete remission of neurotic symptoms among the patients of the first group, without bringing improvement to the patients who complained of depression. The states of anxiety and tension had not developed independently but were mostly associated with the heart disease in the patients of the second group. The results in this group were inconsistent; meprobamate had favorable effect on some patients and no effect on others with the same or a similar clinical picture. All patients of the third group (arterial hypertension) derived benefit from meprobamate at varying degrees. There was a slight decrease of high blood pressure and gradual remission of some subjective symptoms, among which were headache, palpitation, paracusis, nervousness, and irritability. Complete remission of subjective and objective symptoms was observed in patients with a mild form of hypertension. The drug was well tolerated by all patients. A certain amount of somnolence and drowsiness were the only side-effects noted. These disturbances were bypassed by decreasing the dosage of the drug. Meprobamate exerted only a slight or no change on the pulse rate and on the electrocardiograms in this series of patients.

Immediate Therapy for the Acute Attack of Asthma: A Comparison of Epinephrine and Orally and Intravenously Administered Prednisolone. H. H. Pinkerton Jr. and T. E. Van Metre Jr. New England J. Med. 258:363-366 (Feb. 20) 1958 [Boston].

Prednisone and prednisolone provide relief for the asthmatic patient and are free from the salt-retaining qualities that characterize many related compounds. However, relief has not been evident until 6 to 72 hours after onset of therapy, and therefore supplementary use of faster-acting agents, such as epinephrine, has proved helpful. It has been suggested that the intravenous administration of the corticosteroids might shorten the time required to produce relief, and when a form of prednisolone for intravenous use became available, studies to compare the rapidity of prednisolone administered intravenously, prednisolone orally, and epinephrine intramuscularly in providing relief from wheezing in bronchial asthma were undertaken. The studies were carried out in the allergy clinic of the Johns Hopkins Hospital in the months from March, 1956, to February, 1957.

Thirteen patients received intramuscular injections of epinephrine, 13 a single intravenous injection of 33.5 mg. of prednisolone, and 14 a single oral dose of 33.5 mg. of prednisolone. Epinephrine provided more rapid relief from asthma than did prednisolone given either orally or intravenously. There was no significant difference between the responses to prednisolone given orally or intravenously within 3 hours of administration, although the 17-hydroxycorticosteroids occurred almost immediately after the intravenous administration of prednisolone but 1 to 3 hours after an oral dose. This suggests that the initiation of clinical response depends on more than plasma levels. Intravenous injection of prednisolone is useful when the oral route is contraindicated. There was no indication that epinephrine or prednisolone potentiated each other's effect on asthma. This is not surprising in view of the evidence that the effect of epinephrine is sympathomimetic and that of prednisolone anti-inflammatory. It is evident that epinephrine may be used to advantage to supplement prednisolone therapy. Therefore, the effectiveness of epinephrine should be maintained by instituting corticosteroid treatment before excessive use of epinephrine has induced drug resistance (tachyphylaxis).

PATHOLOGY

Demonstration of the Value and the Possibilities of the Official Method of Alcohol Estimation in the Blood by the Control Examinations Provided for by Legislation. H. Griffon and R. Le Breton. Ann. méd. lég. 37:237-247 (Sept.-Oct.) 1957 (In French) [Paris].

The official method used in France for estimating the amount of alcohol in the blood, in which two standard procedures, Nicloux's distillation of blood and estimation of the nitrochromic alcohol by the Cordebard technique, are used, has been criticized on several occasions, not only by operators with little experience but also by expert biologists. The criticisms, however, are generally lacking in validity. Thus, it has been said that the official technique combines macroanalysis and microanalysis and that the quantity of distillate, about 40 ml., is needlessly large. It is true that only 2 ml. (not 1, as stated by the critic, since for accuracy the determinations must always be made in duplicate) is required for the chemical estimation of the alcohol in the distillate, but the other 38 ml. is useful because this amount makes it possible to prove, by the method of extraction of alcohol in a pure state, that the volatile reducing substances estimated by the chemical method are, in fact, composed of alcohol. Proof of this kind is often essential, not only when the analysis of the blood is delayed, as it may be during the vacation period, for example, but also when doubt exists as to its proper preservation and especially when it has been obtained from dead bodies. Mention of this contingency might well be made in the official stipulations.

The technique, now officially adopted, has been in use in the Toxicology Laboratory of the Prefecture of Police for 15 years and has proved to be perfectly adapted to the end in view. It produces results that are remarkably constant and so precise that the order of magnitude of the least favorable comparative error is barely more than plus or minus 5%, which for a biological technique is satisfactory. Determinations of blood alcohol which were made in 31 cases after a lapse of 10 months were perfectly consistent with the estimates initially made in the same cases—a fact which provides additional proof of the value of the method used in determining the blood alcohol and of the legislative measures surrounding such determinations. It would, however, be desirable to have supplementary documents providing for the separation of alcohol in the pure state, whenever the biologist deems it advisable.

and prescribing the procedure to be employed in sterilizing the skin and the equipment and prohibiting the use of volatile reducing substances for this purpose.

Bone Marrow Transplantation in Animals Exposed to Whole-Body Radiation. C. C. Congdon. J. Cell. & Comp. Physiol. 50:103-108 (Dec. [Supp. 1]) 1957 [Philadelphia].

The author discusses experiments in which lethally irradiated animals were kept alive by intravenous injection of normal bone-marrow cell suspension. A quantity of blood-forming cells are removed from the bone marrow of a nonirradiated animal. The living cells are suspended in buffered isotonic solution of sodium chloride and injected intravenously into a lethally irradiated, isologous, genetically identical animal (donor and recipient belonging to the same inbred strain). It was established that blood-forming tissues are specific for irradiation injury. Adult isologous spleen that contains blood-forming cells, fetal liver, bone marrow, and sometimes whole embryos will cause recovery of the lethally irradiated animal, but adult liver, heart muscle, brain, endocrine glands, and other nonhematopoietic tissues will not promote recovery. The dose of hematopoietic cells necessary for recovery depends partly on the genetic relationship of donor and host. A problem of great current interest is whether the immune mechanism is transplanted along with the precursors of blood-forming cells. This is particularly important in trying to understand the delayed foreign bone-marrow reaction. When isologous bone marrow is given to the irradiated recipient, there is good 30-day survival at supralethal doses of radiation; and if the animals are observed for a year or so, there may be no additional mortality. However, bone marrow from a different strain or from a different species, such as transplantation of rat bone marrow to a mouse, may give good 30-day survival, but large numbers of the animals die subsequently.

Recovery from lethal irradiation injury in the bone-marrow experiment is caused by a rapid regeneration of blood-forming tissue that prevents infection, hemorrhage, and anemia. Evidence from chromosomal, histochemical, and immunological techniques demonstrates that the regenerated blood-forming cells and their products in the peripheral blood are descendants of the injected blood-forming elements. When the donor of the bone marrow is not genetically identical to the irradiated recipient, the transplanted bone marrow can be associated with a delayed immunological disorder that kills most of the irradiated mice many weeks after exposure.

Immunological Aspects of Homo- and Heterologous Bone Marrow Transplantation in Irradiated Animals. D. W. van Bekkum and O. Vos. J. Cell. & Comp. Physiol. 50:139-156 (Dec. [Supp. 1]) 1957 [Philadelphia].

In this investigation the effects of homologous and heterologous bone-marrow grafts in mice and rats were studied after roentgen-ray irradiation with various doses. The results show that in mice homotransplantation and heterotransplantation are possible only after supralethal doses of radiation to the whole body. The failure of the transplantation after smaller doses of roentgen rays was thought to be caused by the survival of a few antibody-producing cells. The authors tested this hypothesis by injecting isologous lymphoid cells (from a genetically identical animal of the same inbred strain), together with rat bone-marrow cells, into irradiated mice. By means of various homologous and heterologous host-donor combinations, the authors conducted a quantitative study of the therapeutic effect of bone-marrow transplants in irradiated mice and rats. The results indicated that even after supralethal doses of irradiation the immunological defense system is not fully paralyzed. A delayed mortality occurs during the second and third months after irradiation in mice protected with homologous and heterologous bone marrow. The results of a quantitative study of the effectiveness of isologous, homologous, and heterologous bone marrow show that the number of cells required to protect the host from acute radiation death is related to the degree of antigenic difference between the donor and the host.

If functional grafts of homologous and heterologous bone marrow are to be tested, the recipients have to be submitted to supralethal irradiation of the total body. Even in these animals the defense against foreign tissues is not completely inhibited, but successful transplantation can be obtained when sufficiently large numbers of cells are injected, provided that the antigenic difference is not too great. The assumption that some reaction against the graft remains possible, even after relatively heavy total-body irradiation, is supported by the observation that small numbers of intact isologous lymph-node cells may prevent the successful transplantation of rat bone marrow in irradiated mice. Although irradiated rats could be protected satisfactorily with isologous bone marrow, no therapeutic effect has been obtained with mouse bone-marrow cells.

According to the data obtained on the presence of rat granulocytes and rat erythrocytes in the peripheral blood of mice protected with rat bone marrow, the foreign hematopoietic cells replace those of the host within a few weeks after the transplantation. In some cases, the host's hematopoietic tissues regenerate; this is accompanied by the reappearance of an immunological response against the donor tissues. The delayed mortality is virtually absent after treatment with isologous cells. Transplantation of homologous and heterologous bone marrow causes a high rate of delayed mortality. Only a few delayed deaths were observed in F_1 mice treated with parent-strain marrow and also in C57BL mice treated with F_1 marrow. It is considered likely that the delayed mortality is related to immunological reactions. Theoretically, both antibody production by the host against the graft and, reversely, by the graft against the host's tissues appears possible.

RADIOLOGY

Solitary Pancreatic Lithiasis. H. Cosco Montaldo. An. Fac. med. Montevideo 42:63-71 (May-Aug.) 1957 (In Spanish) [Montevideo, Uruguay].

Two cases of true solitary calculi of the duct of Wirsung are reported. The patients were women, aged 19 and 46 years respectively. In neither of the patients was a definite clinical diagnosis of pancreatic lithiasis made. The younger patient had symptoms of acute cholecystitis without jaundice. A cholecystography gave negative results. A cholecystectomy, a choledochotomy, and a retroduodenal-pancreatic décollement were performed. A calculus the size of a grain of corn, lodged at the pancreatic duct, was palpated and removed by duodenectomy and papillectomy. The gallbladder and the common bile duct did not contain any calculi. The patient was discharged in perfect condition. The older patient had symptoms of cholelithiasis with jaundice. A cholecystography gave negative results. A cholecystectomy, a choledochotomy, and a retroduodenal-pancreatic décollement were performed. The calculus palpated in the pancreatic duct was misjudged as if it were a pancreatic nodule of the head of the structure. It was left untouched. The gallbladder removed by operation contained 40 stones. A few days after the operation, while the cholecystogram was being reviewed, the image of a calculus, either pancreatic or at the common bile duct, was observed. Morphi-amylo-cholangiography was done 17 days after the first operation. It gave the clearest image of a calculus, which was lodged in the lumen of the pancreatic duct. The calculus was not removed, and it was asymptomatic. Morphi-amylo-cholangiography was again performed on the patient 2 years after the first operation. It showed that the calculus persisted unchanged in the same location and position as it was when observed the first time. The patient is in perfect condition.

The author directs attention to the importance of (1) retroduodenal-pancreatic décollement during biliary surgery which permits palpation of pancreatic calculi and (2) morphi-amylo-cholangiography for roentgenologic visualization of pancreatic calculi. Retroduodenal-pancreatic décollement in the course of biliary surgery is made by (1) opening of the peritoneum at the level of the external border of the upper half of the second portion of the duodenum, (2) décollement of this border in an extension of 5 or 6 cm., and (3) introduction of the index and middle fingers of the right hand for palpation of the pancreas and extrinsic palpation of the pancreatic ducts. The technique of morphi-amylo-cholangiography involves (1) giving the patient an injection of 1 cc. of morphine 10 to 30 minutes before administering the opaque substance, (2) taking 2 or 3 serial pictures at intervals of 3 to 5 minutes during the stage of spasm of the sphincter of Oddi induced by morphine, (3) giving the patient an ampul of amyl nitrite to inhale, and (4) taking 2 or more pictures during the stage of relaxation of the sphincter of Oddi produced by amyl nitrite. Cholangiography during the opposite stages of spasm and relaxation of the sphincter of Oddi permits a clear visualization of the whole biliary and pancreatic ductal systems. The author shows by an illustration the results of morphi-amylo-cholangiography in 1 patient whom he had observed personally. The illustration shows the complete filling of the biliary ductal system by the opaque substance and, by reflux, the filling also of the duct of the main and the accessory pancreatic ducts, giving a clear lacunar image of a solitary calculus lodged at the main duct. This is believed to be the first record of the sort in the cholangiographic literature of the world.

A Year's Experience with a Co ^{60} Radiation Therapy Unit. G. Cooper Jr. and J. M. Carter. Virginia M. Month. 85:118-123 (March) 1958 [Richmond].

The authors discuss the physics of the radioactive cobalt (Co ^{60}) unit and enumerate its several advantages over orthovoltage (250 kv.) roentgen-ray irradiation. They commenced to treat patients with the Co ^{60} unit in July, 1956, and at the end of a year they had completed treatment of 231 patients with 236 tumors. Sixty-six of the tumors were in the head or neck, 41 in the thoracic cavity, 43 in the abdominal cavity, 60 in the pelvic cavity, 15 in the skeleton, and 11 in other locations. The comparison of Co ^{60} radiation with orthovoltage irradiation must obviously be confined to immediate effects, since long-term results will not be available for several years. In the meantime it can be stated that the Co ^{60} beam makes it possible to introduce into subsurface lesions significantly larger tumor doses, to introduce the same tumor dose in fewer days, and to accomplish these 2 important advances with little or no skin reaction and with much less bone-marrow depression and radiation sickness. The result is better palliation of incurable malignancies and perhaps a little higher cure rate. Radiation of the energy order of the Co^{60} beam is to be preferred to orthovoltage irradiation in the treatment of tumors in the head and neck and in the thoracic, abdominal, and pelvic cavities whenever a large tumor dose is needed. The same is true of deep-seated tumors in the musculoskeletal system which need a large tumor dose. When it is necessary to introduce radiation through skin damaged by previous radiation, advantage can be taken of the skin-sparing effect of the high-energy, homogeneous beam, even though the tumor dose needed is not large and even though the lesion is immediately subcutaneous. The bone-sparing effect of the high-energy, homogeneous beam is particularly useful when children's skeletons with their highly susceptible growth zones have to be placed in a beam of ionizing energy.

Complications of Aortography: Factors Influencing Renal Function Following Aortography with 70 Per Cent Urokon. A. C. Beall Jr., E. S. Crawford, C. M. Couves and others. *Surgery* 43:364-380 (March) 1958 [St. Louis].

The increased number of reports in the literature on complications, predominantly renal, occurring after aortography, which has been commonly considered an innocuous procedure, prompted the authors to conduct studies on 51 female dogs and on 18 men and 1 woman, between the ages of 36 and 70 years, in an attempt to elucidate the factors related to the development of functional renal changes and renal damage after aortography. Determinations of glomerular filtration rate, renal blood flow, and water and electrolyte excretion were recorded. A 70% solution of sodium acetrizoate (Urokon) was used as contrast medium. Three variables with respect to its administration were investigated: (1) dosage used, (2) site of injection, and (3) alteration in hemodynamics in the region of the kidneys.

Observations made both in the animals and in man indicated that the immediate hemodynamic response of the kidney to sodium acetrizoate is vasoconstriction. This is manifested by depression of both the glomerular filtration rate and the renal blood flow. In the dog, this was only slightly more pronounced if the aorta was occluded below the renal arteries in the course of the injection of the contrast medium. In man, chronic occlusion below the renal arteries due to arteriosclerotic occlusive disease does not appear to predispose the patient to renal damage after the intra-aortic injection of sodium acetrizoate. Some persistence of the acute renal hemodynamic response was seen in both man and animal as long as 2 hours after aortography. Return to normal occurred in most instances after several days, unless the amount of contrast medium injected was large enough to produce anatomic and functional damage to the kidney. Accuracy in placement of the aortographic needle is of utmost importance. The injection should be made into the suprarenal portion of the abdominal aorta, since direct injection into the renal artery produces severe damage to the kidney. Apparently because of inherent vasoregulatory mechanisms in the renal circulation, renal blood flow is not increased after aortic occlusion distal to the renal arteries. Therefore, there is no increase in the contrast medium delivered to the kidney after injection of this material when aortic occlusion is present. However, when the sodium acetrizoate is injected directly into the renal artery, the entire dose reaches the kidney since there is no collateral circulation to bypass this organ.

It is considered highly significant that renal damage did not occur in 200 patients in whom aortography was performed by the authors with a dose of 25 cc. or less of 70% solution of sodium acetrizoate, unless the renal artery was directly injected. Renal damage occurred in 7 of the 100 patients who received more than 30 cc. of the contrast medium at an earlier time when proper dose was not appreciated. It would appear reasonable not to expect renal complications when doses of a 70% solution of sodium acetrizoate of 30 cc. or less are employed and direct injection of the renal artery is avoided.

PHYSIOLOGY

Effect of Weight Loss on Respiratory Functions. *J. Salzano, R. V. Gunning, T. N. Mastopaulo and W. W. Tuttle. J. Am. Dietet. A.* 34:258-264 (March) 1958 [Chicago].

Because of the paucity of information regarding the effect of weight reducing on physiological responses, this investigation was undertaken to determine the effect of weight loss on some respiratory functions. Studies were made on 12 women and 4 men, ranging in age from 22 to 37 years. Weight of the subjects ranged from 14 to 85% above average. Nutritionally adequate diets were used to produce a decrease in body weight calculated to proceed at the rate of 2 lb. per week. The following functions were studied before, during, and after the weight-reducing regimen: respiratory rate, tidal volume, minute volume, and oxygen consumption, at rest. In addition, the oxygen required to perform a given amount of work (1,250 kg.-m. per minute and 720 kg.-m. per minute for the men and women, respectively) was calculated. The resting respiratory rate was not significantly changed in the majority of the subjects by a reduction in body weight. The majority of the subjects showed no significant change in resting tidal volume. However, 6 subjects had a resting tidal volume which was significantly less than control, and 1 subject showed an increase.

Weight reduction was not followed by any significant change in resting respiratory minute volume in the majority of the subjects. Ten subjects had significantly less resting oxygen consumption after weight loss, while 6 subjects showed no change. Ten subjects showed no change in resting oxygen requirements, calculated on the basis of milliliters per kilogram of body weight; 6 showed an increase. The oxygen required to perform a given amount of work was significantly decreased during the post-reduction phase of the experiment. A reduction in body weight was followed by a significant decrease in the oxygen required to perform a given amount of work when body weight was used as a metabolic reference standard in 10 subjects; in 6 subjects, there was no change. The oxygen debt caused by work performance expressed as milliliters was significantly reduced in 12 subjects; in 4 it was unchanged. Oxygen debt, expressed as milliliters per kilogram of body weight, was decreased in 9 subjects after weight loss; in 7 no consistent change was seen.

Size and Shape of the Gallbladder and Volume of the Liver in Immature and in Full-term Newborn Infants and in Infants in the First Year of Life. R. Bulgarelli and E. Bertolotti. Minerva pediat. 9:1512-1519 (Dec. 8) 1957 (In Italian) [Turin, Italy].

Capacity, shape, position, and malformation of gallbladder have been studied in 130 infants since 1955. Of these, 76 were immature newborn infants, 22 were full-term newborn infants, and 32 were infants in the first year of life. The authors define as immature those infants born before or during the 9th month of gestation and weighing not more than 2,500 Gm. (5½ lb.) at birth. During the first month of life the capacity value of the gallbladder in this series of infants was found to be 2.26 cc., the mean length value 3.8 cm., and the mean width value 1.4 cm. The gallbladder had a cylindrical shape in the immature and a pear-like shape in the full-term newborn infants. The lower limit of the gallbladder did not reach the lower surface of the liver in about three-fourths of the immature newborn infants; it did reach in slightly more than one-half of the full-term infants and infants in the first year of life. Among the 352 autopsies performed during the last 2 years, 2 instances of intrahepatic gallbladder were found. The gallbladder exceeded the physiological limits in 4 infants and was below these limits in 11. The left lobe of the liver decreased in volume and the right lobe increased in these infants during the first week of life. The ratio of the liver weight to the body weight gradually decreased in the immature newborn infants during the period between the 6th and the 9th month of gestation (from 4.44 to 3.45%). This ratio increased in the full-term newborn infants (4.1%) and gradually and slowly decreased afterwards until the third month of life was reached (3.97%).

PUBLIC HEALTH

The Caravan Problem. H. Mackenzie-Wintle. Med. Officer 99:119-120 (Feb. 28) 1958 [London].

The author made a survey of trailers (caravans) in the south Oxfordshire district. A questionnaire, as noncontroversial as possible, was sent to the owners of 498 trailers on sites and to 332 persons whose trailers were currently registered on individual licenses in the area. To this questionnaire only 38% replied in spite of an assurance that, since the forms asked neither the name nor the address of the replier, he or she could not be traced. Site-owners who were sent a copy cooperated in almost all cases. Almost half of the trailers were occupied by couples. The next largest group (23%) consisted of couples with 1 child, followed by people living alone (14%). These 3 groups comprised almost 85% of the total. Two trailers had 4 children each, 8 trailers had 3 children each, and 28 trailers had 2 children each. Reasons given for starting to live in a trailer were housing shortage (30%), financial reasons (16%), desire to be independent (14%), preferred living in trailer to living in rooms (11%), need of mobility because of job (9%), and other reasons (20%). In answer to the question: "If you could have a new house at a rent you could afford and not lose money on selling your trailer, would you take the house or stay in the trailer?" Sixty per cent would prefer a house, 33% would prefer a trailer permanently, and 7% gave indeterminate, illegible, or uninterpretable answers.

Summarizing his own views about trailers, the author states that they are not suitable for children; that they are always substandard housing accommodation, and the fact that people can acquire a taste for trailer living does not alter this fact; that trailer living probably causes most young couples to postpone having a family or limiting their family to an only child, both of which are undesirable; that in his own districts he gets about twice as many complaints of sickness being caused by living conditions in trailers as in houses; and that the law with regard to residential trailers is inadequate. The author admits, though, that for young couples, with both the husband and the wife working, trailer living is better than living with in-laws or in digs and that trailers often afford suitable accommodation for older persons. Housing authorities should on no account slacken their efforts to provide houses because of the number of people living in trailers; most of them are in trailers because they have to be, not because they want to be. The author suggests more comprehensive legal regulations on residential trailers than are now in force under the Public Health Act.

BOOK REVIEWS

A History of Nutrition: The Sequences of Ideas in Nutrition Investigations. By Elmer Verner McCollum. Under editorship of H. Bentley Glass. Cloth. $6. Pp. 451. Houghton Mifflin Company, 2 Park St., Boston, 1957.

Although to encompass the entire history of the science of nutrition in a book of 450 pages is an almost insurmountable task, the author, who has been responsible for much of the present knowledge of nutrition, has managed to do this admirably. The subtitle of the book gives one an insight into the type of material included. The author spent about 10 years reviewing the published literature of the last 200 years for the background material for this book and has confined his history to those thoughts and experiments which, in his opinion, opened new areas of discovery. The period covered is roughly the 200 years between 1740 and 1940. The author designates 1940 as the end of an era. Essentially, that was about the time in which the primary objectives delineated by the early workers in the field of nutrition were achieved, i. e., determination of what chemical substances constituted an adequate diet for man and domestic animals.

The author traces the development of new ideas concerning the constituents of foods and of the gradual realization of the relation of foods to health. In 1745, it was believed that man, except for the spiritual portion of his being, consisted of wheat gluten. As recently as 1900, it was the generally accepted belief that only carbohydrate, fat, protein, and certain inorganic salts were all that need be considered in determining the adequacy of the diet. In speaking of the great strides made in the science of nutrition, the author says, "The new knowledge brought about improvement of health and its attendant elevation of the status of human life above the sordid, to a degree scarcely equalled by any other agency concerned with the prevention or cure or disease. . . . Viewed from this standpoint, the rise of the science of nutrition is one of the greatest events in human history." A list of basic references follows each chapter. This book would be a valuable addition to the library of every physician, as well as to those of dietitians, nutritionists, teachers, and all concerned with the science of nutrition.

Spezielle chirurgische Therapie. Von. Prof. Dr. Max Saegesser. Band II, Sammlung medizinischer Lehr- und Handbücher für Ärzte und Studierende. Fifth edition. Cloth. 128 marks. Pp. 1,476, with 2,384 illustrations. Verlag Hans Huber, Marktgasse 9, Bern 16, Switzerland; [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1957.

This textbook of general surgery, written in German by a Swiss surgeon, is printed on paper of high quality, and the print is large and the binding excellent. The material is divided into 10 parts, including injuries and diseases of the head, injuries and surgical conditions of the neck, thoracic surgery, abdominal surgery, urology (male), surgery of the spinal cord and vertebrae, general surgical conditions of the extremities, surgical diseases of bones and joints, injuries to bones and joints, and, as a final part, delirium tremens and a general philosophical discussion on the management of the dying patient. This last chapter is most appropriate to a textbook of surgery, although no other treatise of surgery has included such material. All the subjects are dealt with in an up-to-date manner. There is no bibliography, but frequent allusions by name are made to well-known contributors to the current surgical literature of Europe and the United States. One of the outstanding features of the volume is the line drawings which profusely illustrate the text. For the practitioner who is familiar enough with German to be able to read this book without frequent recourse to a dictionary, it should afford a complete review of general surgery (neurosurgery and gynecology excluded). For the surgeon studying German, a perusal of this compendium would enable him to combine practice in reading this language with a review of the broad field of general surgery.

A Handbook on Diseases of Children Including Dietetics & the Common Fevers. By Bruce Williamson, M.D., F.R.C.P. Eighth edition. Cloth. $6. Pp. 483, with 117 illustrations. E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, Scotland; Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1957.

The eighth edition of this handbook of children's diseases has been revised and in part rewritten since its last edition was published four years ago. The sections on antibiotics and poliomyelitis have been brought up to date. The inclusion of appropriate treatment with steroids (except that such treatment is not mentioned for fulminating meningococcal in-

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

fections), the use of recently available orally given nonmercurial diuretics, and the mention of increasing caution with respect to the degree to which children are exposed to radiation are indications of most recent pediatric thought, but no mention can be found of the use of such valuable new drugs as reserpine and other tranquilizers. Some of the treatments recommended, such as the use of castor oil as a cathartic and radiation therapy for an enlarged thymus gland, are largely outmoded in this country. This book is essentially a miniature textbook, in that it attempts to cover the disorders of all the body systems of the child. This makes it possible to give only the highlights of the more common disorders and precludes even mention of many of the unusual conditions that the reader might seek in such a handbook. A section on disorders of the newborn infant is noticably lacking in information on the severe illnesses arising from disorders of the respiratory tract and central nervous system. More emphasis might have been given also to the special problems of the immature infant, since better care for this group offers the greatest hope of reducing infant mortality rates. The illustrations are numerous and excellent. The small size, easily readable print, and soft covers make it well suited for its purpose of a handy reference on pediatrics for the medical student, nurse, and general practitioner.

Operative Surgery. Volume Six: Hand, Amputations, Plastic Surgery, Gynaecology and Obstetrics. Under general editorship of Charles Rob, M.C., M.Chir., F.R.C.S., Professor of Surgery, St. Mary's Hospital, London, and Rodney Smith, M.S., F.R.C.S., Surgeon, St. George's Hospital, London. Cloth. $19.50. Various pagination, with illustrations. Butterworth & Company, Ltd., 88 Kingsway, London, W. C. 2, England; 1367 Danforth Ave., Toronto 6, Canada; [F. A. Davis Company, 1914-16 Cherry St., Philadelphia 3], 1958.

The editors have continued the policy of selecting outstanding British consultants and contributors in the preparation of this reference book. The format is attractive and conforms to that of the preceding volumes. Descriptive, accurate, and informative drawings are numerous and well placed. Each operative procedure is approached in a uniform manner by a description of the preoperative management, the operation, and the routine and special postoperative care. The authors have chosen their references chiefly from British publications. With such a large undertaking (an eight-volume compilation), references from the world literature would add character to the work. By cautious and thoughtful editing, the usual errors of multiple authorship have been avoided and a consistency of style has been maintained throughout. This publication fills a gap in the existing literature, and it is recommended for postgraduate students and residents and surgeons in nonteaching centers.

The Essence of Surgery. By C. Stuart Welch, M.S., M.D., Ph.D., Professor of Surgery, Albany Medical College of Union University, Albany, N. Y., and Samuel R. Powers, Jr., A.B., M.D., M.Sc.D., Professor of Experimental Surgery, Albany Medical College of Union University. Cloth. $7. Pp. 320, with 50 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1958.

A stimulating aspect of this excellent textbook is that operative surgery is discussed on the level of simplified basic factors with disregard for the present-day trend of superspecialization. The thesis that specific principles of surgery do not change regardless of the area under discussion is lucidly expounded. Although a surgical textbook can rarely be read from cover to cover, this book can be with interest and ease. It would be difficult to single out any one of the 12 chapters as being better than any other. The subject of body fluids and electrolytes is difficult to present, but the chapter dealing with loss of body fluids makes the subject understandable and interesting, and the following chapter, which discusses infection, comes to life with a freshness of style that is seldom seen in modern textbooks. The simple line drawings are custom made to the written material and depict the story with finesse. The authors are to be congratulated for writing a book than can be recommended unreservedly.

Shock and Circulatory Homeostasis. Transactions of fifth conference, November 30, December 1, and 2, 1955, Princeton, N. J. Edited by Harold D. Green, M.D., D.Sc., Professor of Physiology and Pharmacology, Bowman Gray School of Medicine, Wake Forest College, Winston-Salem, N. C. Cloth. $4.75. Pp. 337, with 78 illustrations. Josiah Macy, Jr. Foundation, 16 W. 46th St., New York 36, 1957.

The 35 participants of this conference on shock and circulatory homeostasis included internists, surgeons, physiologists, pharmacologists, and biologists. The conference dealt primarily with the following subjects: experimental shock in relation to hepatic blood flow, bacteria, protection by chlortetracycline, germ-free rats, adrenergic, cholinergic, and ganglionic blocking agents, humoral factors, hepatic ferritin systems, hypothermia and chlorpromazine, and lymphatic adjustments. This book enables a large audience to share in the findings of this as in previous Macy conferences. The recording of the informal discussions gives the reader a sense of having been present at the conference. Particularly worthy examples of this are the discussions of criteria of tissue anoxia (p. 21) and of health (pp. 141-144). This should be read by all investigators interested in experimental shock and related phenomena. It is also recommended to those clinicians who enjoy periodic forays into the frontiers of biological and medical knowledge.

QUESTIONS AND ANSWERS

TUBERCULOSIS AND SUNLIGHT

To the Editor:—*A patient who has had active pulmonary tuberculosis, now arrested, is under the impression that she must avoid direct sunlight. Accordingly, she bundles up, regardless of how warm the weather, to avoid the sun. Is there any basis for such precautions?*

H. L. Herschensohn, M.D., Santa Monica, Calif.

Answer.—Sunlight has been employed in the treatment of tuberculosis since antiquity. During the early part of the present century, there were those who extolled its value as a therapeutic agent and those who opposed its use on the ground that it results in increased symptoms, including hemoptysis. LoGrasso and Balderrey conducted a carefully controlled and well-documented study (*Am. Rev. Tuberc.* 10:117, 1924). Prior to that time, personal opinion, too few and too short periods of observation, too much exposure, and other factors had resulted in the controversy. The LoGrasso and Balderrey study resulted in the following statement: "According to our experience, heliotherapy will not produce hemoptysis, increase the activity of the lesions, or reactivate it if judiciously employed." These workers reported that patients with pulmonary tuberculosis derived considerable benefit from heliotherapy when promptly administered. Despite these observations, the opinion still is sometimes expressed that sunlight is harmful, even to persons with arrested tuberculosis. However, there is no documented evidence that by avoidance of direct sunlight this patient is protecting herself against activation of the arrested disease. Long periods of exposure of the entire body to direct sunlight, resulting in sunburn, would not be good for her or anyone else. However, the amount of sunlight that reaches exposed surfaces in ordinary street clothing will cause her no harm.

PENICILLINS G AND O

To the Editor:—*What are the relative values of penicillin G and penicillin O?*

R. B. McBride, M.D., Dallas, Texas.

Answer.—Penicillin G is benzyl penicillin and is obtainable either as the sodium or potassium salt, as procaine penicillin G, or as benzathine penicillin G. The chief difference is in effectiveness and duration of action; procaine penicillin G persists in action about six times as long as penicillin G, whereas benzathine penicillin G lasts for about 30 times as long as penicillin G from equivalent intramuscular dosage. Potassium penicillin O is allylmercaptomethyl penicillin. There is not as much information available on penicillin O as on penicillin G. It does seem to have less allergic tendencies. Cautious trial of penicillin O is justified in patients sensitive to penicillin G in special conditions when penicillin treatment is necessary. The chief difficulty developing with penicillin G is an apparently increasing tendency to produce allergic reactions.

SJÖGREN'S SYNDROME

To the Editor:—*A woman, aged 30, has complained of burning, itching, and dryness of the eyes for about two and one-half years. In addition, she complains of dryness of the mouth and nose to a lesser degree. Even crying does not produce lacrimation. There is no disturbance of vision. The diagnosis has been Sjögren's syndrome. Treatment has consisted of methylcellulose, prednisone ophthalmic drops, pilocarpine given by mouth, various topical anesthetics, estrogen injections, prednisone and prednisolone, and orally given vitamin A. She has also avoided strong light and irritants, such as tobacco smoke and dust. To the time of writing, no benefit has been obtained with these measures. Please advise regarding additional therapy.*

M.D., Pennsylvania.

Answer.—Sjögren's syndrome consists of dryness of the eyes, nose, mouth, and throat, due to deficient secretion of the appropriate glands, with the frequent association of enlarged parotid glands and rheumatoid arthritis. The sex (90% female) and age (majority postmenopause) incidence suggests hormonal imbalance, and other factors frequently considered include nutritional deficiency, metabolic dysfunction, and rheumatic diathesis. However, the etiology remains obscure, and treatment is symptomatic. Histologically, the lacrimal glands show round cell infiltration and atrophy of secretory elements, with eventual fibrous scar tissue replacement. The severity of symptoms and the difficulty of treatment are proportional to the amount of functioning gland tissue remaining and the tear flow produced. Schirmer's test, with use of strips of Whatman's filter paper 5 mm. wide, gives the most convenient measure of lacrimal function. The nor-

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

mal tear production is considered to be 15 mm. or more of moistening in five minutes. As little as 5 or 6 mm. may be wet with few or no symptoms, but in severe cases there may be less than 1 mm. In refractory cases of markedly deficient tear production, extirpation of all four lacrimal canaliculi affords the best relief by promoting retention of what scanty tear flow is present and increasing the effectiveness of artificial tears. The technique is as follows: The area of the canaliculi is infiltrated with procaine hydrochloride injected with a fine needle. Both upper and lower puncta are dilated. The electrocautery needle is introduced 6 to 8 mm. into each canaliculus, and coagulation is produced. Occasionally, repetition of the procedure may be necessary. Care must be taken, especially in young patients, to ascertain that tear flow is actually impaired, or a permanent and annoying epiphora may result. Epiphora is rare if there is less than 5 mm. of tear production as measured by Schirmer's test.

CALCIFICATION OF INTERVERTEBRAL CARTILAGES

To the Editor:—*In a patient with a diagnosis of calcification of intervertebral cartilages, possibly due to some activity, what therapy would help retard this ailment?* *M.D., Wisconsin.*

Answer.—Calcification of intervertebral cartilages is an incidental finding and is of no clinical significance, unless x-ray evidence shows that it actually protrudes. It represents only an end-stage in development. It is suggested that the inquirer look elsewhere for the cause of the condition for which he is treating this patient.

MYOCARDIAL INFARCTION AND RETIREMENT

To the Editor:—*A 63-year-old school bus driver was referred for an opinion as to recommendation for retirement. In July, 1957, he was stricken with typical symptoms of myocardial infarction, which was substantiated by an electrocardiogram. Since the original episode, he has been asymptomatic. He has lost 15 lb. but remains slightly obese. He has had no symptoms suggestive of cardiac disease. Physical findings are completely normal. The only evidence of the previous disease is in the electrocardiogram, which demonstrates a QS complex in leads V_3 and V_4. He does not wish to retire. Please comment as to whether this man should be permitted to continue driving a school bus.*

M. D. Reiter, M.D., Wheeling, W. Va.

Answer.—This question poses a social problem as well as a medical one. In answer to the medical portion of the question, the patient should be allowed to continue to work at a suitable occupation. From a medical standpoint, the effort involved in driving the school bus seems ideally suited to one who has recovered successfully from a myocardial infarction, but the wisdom of allowing such a patient to continue in such a job might be questioned for other reasons. This job places the safety and even the lives of other persons directly in his custody. Should a recurrent myocardial infarct result in disaster, criticism might justifiably be leveled at the person or persons who permitted this patient to continue in such an occupation.

Answer.—This question is not as simple as it seems. Such patients should return to their jobs, provided they do not endanger the lives of others. Certainly people who have recovered from episodes of coronary occlusion drive cars all the time, but once a man has sustained an acute coronary occlusion, he may develop another. Thus, the question is complicated by moral, legal, and compensation insurance aspects. For this reason the patient should not be permitted to return to any employment, such as driving a school bus, where the lives of others are in his hands.

PROTEIN-BOUND IODINE TEST

To the Editor:—*How can the protein-bound iodine test be declared an accurate measure of thyroid activity when there appear to be so many more or less imponderables connected with the patient's intake of iodine? These include the intake of iodized salt in quantities that are not too accurately measured and the frequent self-medication with vitamin-mineral combinations which contain iodine. Is the intake of iodine negligible in connection with this test? Should the patient be told to avoid these iodine-containing substances before having a protein-bound iodine determination done? If so, for how long?*

Paul E. Adolph, M.D., Wheaton, Ill.

Answer.—Ingestion of inorganic iodide may lead to a falsely and abnormally high protein-bound iodine value. Iodide ion combines loosely with serum albumin when circulating in high enough concentration and for sufficient time. This combination is precipitable with the protein precipitants used in the chemical procedure. In general, several milligrams of iodine must be ingested daily for a number of weeks before any significant increase in the protein-bound iodine level will result. No definite information is available about the time required to avoid this effect of iodide ingestion prior to a protein-bound iodine test, but probably three or four weeks is enough. However, in actual practice, high protein-bound iodine values are seldom seen from vitamin or iodized salt usage. The use of the butyl extractable iodine procedure, now clinically available, will circumvent the artefact created by iodide ion. The iodide is extracted from the carrier protein by this solvent but is removed by an alkaline or other wash. Organic iodinated compounds are detected by both the protein-bound iodine and butyl extractable methods, and falsely high values are found when these compounds are present in the circulation.

UNSATURATED FATTY ACIDS FOR HYPERCHOLESTEREMIA

To the Editor:—*Please give information on the value of corn oil and sunflower oil in the treatment of hypercholesteremia. In what form and in what amounts should they be taken?*

M.D., New Jersey.

Answer.—Dr. Ahrens, of the Rockefeller Institute of New York, has found that the use of unsaturated fatty acids in the amount of 30% of the total caloric intake, under rigidly controlled dietary restrictions, will lower the blood cholesterol levels in those patients exhibiting hypercholesteremia. A reprint of the symposium on the subject of fats in nutrition, sponsored by the American Medical Association's Council on Foods and Nutrition and held in New Orleans in 1957, is available from the Council. Sunflower oil and corn oil are similar in their content of unsaturated fatty acids. About 90% of the oil consists of linoleic acid and oleic acid in a proportion of about 2 to 1. In giving such products to patients, it must be remembered that they are fats and, as fats, are a source of calories. Therefore, instead of adding them to the regular diet, it would probably be desirable to insert them into the diet in place of some of the fats now being used. It is emphasized that these products are still in the experimental stage and that there are bound to be wide variations among individuals in their responses to this type of therapy.

"KNOCK-OUT" DROPS

To the Editor:—*What is the composition of "knock-out" drops? Are they the result of someone's imagination and portrayed by theatrical people and novelists? What is the composition of any type of medicament which, added to a liquid (such as coffee or milk) or given separately, will produce rapid sleep hypnosis? In many instances, when treating patients it is necessary to give a rapidly acting hypnotic by oral administration when the hypodermic cannot be used. One patient, who is allergic to chloral hydrate and who is so emotionally unstable as to require a very rapidly acting "knock-out" type of medication, is afraid of hypodermic needles.*

M.D., Maryland.

Answer.—"Knock-out" drops are very real; chloral hydrate in solution can be added to an alcoholic beverage which covers the taste of the drug so sufficiently that the drinker, who probably has already had several drinks, is unaware of the drug. This consultant is not aware of any magic formula which, taken orally, will effect sleep rapidly without the patient being aware of its presence. As a general rule, those substances (with the possible exception of chloral hydrate), taken in therapeutic doses, which effect sleep quickly have an action of relatively short duration. Secobarbital sodium is bitter in solution. Whether the "allergy" of the patient is actually a dislike for the taste of the chloral hydrate, which can be given in capsule form, or a response to gastric discomfort, since the drug is irritating, is not stated. Actual allergy to the compound is rather rare. The irritation may be overcome by proper dilution.

PROPHYLAXIS OF AMEBIASIS

To the Editor:—*In the comment on prophylaxis of amebiasis, which appeared in the Queries and Minor Notes section of* The Journal *for Nov. 16, 1957, page 1518, the following advice was offered: "If diarrhea develops, bed rest, the frequent consumption of tea, rice, and applesauce, and the use of simple antidiarrhea measures, such as kaolin with pectin or bismuth preparations and possibly camphorated opium tincture (paregoric), will permit the disease to run its brief course...." This advice should never be taken without reserve, for, though apparently innocuous, it may lead to very serious consequences. First of all, the term diarrhea denotes a symptom which may be part of a mild disease not yet classified, or, in the countries where amebiasis prevails, it may be among the first symptoms of a very serious condition, such as paratyphoid, bacillary dysentery, nonspecific gastrointestinal infections, or even food poisoning. How would one know what the diarrhea is going to develop into? The course of this disease may be brief; the lives of the patients may be equally as brief. Second, "refractory amebiasis," mentioned in the comment, if properly treated when the first symptoms appear, rarely becomes refractory. It is the policy of waiting which causes amebiasis to be refractory. In like manner, bacillary dysentery, if not treated properly at the onset, not infrequently continues into very troublesome chronicity. It might be difficult for physicians not in the tropics to identify cysts of Entamoeba histolytica, but when the disease is in the symptomatic stage, when mobile trophozoites usually abound, most physicians in the tropics can usually spot one in a matter of minutes. Why wait until the disease is chronic and difficult to diagnose and to treat? Is this a medical Monroe's doctrine?*

C. L. Chen, M.D.
Nakon Pathom
Thailand.

WASHINGTON NEWS

FROM THE WASHINGTON OFFICE OF THE AMERICAN MEDICAL ASSOCIATION

Medicare Progress in the House . .
Social Security Hearings Starting . .
Congressional Poll Against Forand Bill . .
Dr. McGuinness Sees More
Research Spending . .

CONFERENCE COMMITTEE TO HAVE FINAL WORD ON MEDICARE CHANGES

Efforts to save Medicare from destructive changes have shifted to the Senate, after House leaders agreed to work out in conference with the Senate modifications that will "make everybody reasonably well satisfied."

The key committeemen in the House went on record as agreeable to lifting some of the proposed Medicare restrictions during debate on the Defense Department's appropriation bill. Their concession came after scores of letters and wires were received on Capitol Hill from state medical societies and individual doctors, all protesting the proposed cut in Medicare funds and proposed limitation of freedom of choice of doctors and hospitals. Communications along the same line also were received from hospital directors.

The House Appropriations Committee had cut funds for Medicare's civilian phase from a requested $71,900,000 to $60,000,000 and at the same time had instructed the Defense Department not to spend more than that amount for civilian hospital and medical care.

This would wipe out civilian Medicare in all areas near military medical installations, because to stay under the ceiling Medicare's directors would have to order these dependents to use military facilities. Such a limitation also would require a complete change in the operating concept of Medicare, including the renegotiation or cancellation of contracts.

Because of legislative complications, the restrictions were left in the appropriations bill as it passed the House. But at the same time Chairman George H. Mahon (D., Texas) of the subcommittee that handled the Defense money bill proposed that the Senate make the necessary changes in the bill, after which a final version would be adopted in the Senate-House conference committee.

At the close of debate on this, Mr. Mahon said: "I think that our service personnel have no need for alarm or undue concern about the action of the committee. I have no doubt but that this will be worked out in the next few weeks in such a way that everybody will be reasonably well satisfied. There is no desire to do any injustice to anyone or to negate the law of the country."

The committee had put in the restrictions in the mistaken belief that care in military facilities is much less expensive than in civilian and that Medicare was costing more than Congress had anticipated. The idea was that by cutting the appropriation the Defense Department would be forced to make greater use of military facilities, which already handle about 60% of all dependents.

Mr. Mahon first indicated his willingness to drop at least some of the restrictions when he was questioned about them by Rep. Melvin Laird (R., Wis.), who introduced letters written to all subcommittee members by Drs. F. J. L. Blasingame, General Manager of the A. M. A., and W. J. Kennard, Acting Director of the A. M. A. Washington Office, and Kenneth Williamson, associate director of the American Hospital Association and head of its Washington bureau. Mr. Laird questioned the effect of the stiff cut in funds. Mr. Mahon replied:

"It does seem to me that if the services can establish that $60 million will not be adequate within the procedure relating to freedom of choice . . . then before this bill is enacted into law finally, an opportunity will be available to present the case to the other body (the Senate) for consideration, I am sure, and the final amount can be worked out in the conference on the bill. It is not the desire of the committee to deny to any military dependents the medical care made available to them under the dependent medical care act."

During the debate Rep. Paul J. Kilday (D., Texas), who sponsored Medicare when it was enacted in 1956, took the floor to protect the program against the committee's amendments. After Mr. Mahon explained that Senate changes would receive friendly consideration in the conference committee, Mr. Kilday accepted the arrangement.

HEARINGS SCHEDULED ON FORAND, OTHER SOCIAL SECURITY MEASURES

Hearings are getting under way before the House Ways and Means Committee on a wide range of bills amending the Social Security Act. Chairman Wilbur Mills (D., Ark.) estimated there are 400 measures pending, including the controversial proposal of Rep. Aime Forand (D., R. I.), for free hospitalization and surgical services for social security beneficiaries.

Sessions, which are expected to run to June 27, open June 16 with testimony from administration witnesses, including Secretary of Health, Education, and Welfare Folsom and Secretary of Labor Mitchell. The American Medical Association witnesses will include Dr. Frank Krusen of the Mayo Clinic, Chairman of the A. M. A. Council on Medical Physics.

(Continued on next page)

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The Forand bill authorizes the Secretary of HEW through negotiations to set charges for physicians, hospitals, and nursing homes, with only those doctors agreeing to participate being eligible to care for patients. The A. M. A. feels that eventually these same benefits would be extended to lower age groups, resulting in time in total federalized medicine. It also is believed that the proposal would spell the end of voluntary health insurance, which has grown considerably in recent years.

Mr. Mills' announcement of the hearings pointed out that due to the short time available and the advanced status of this session of Congress, "it might not be possible for the committee to act on all the proposals on which testimony is presented but that the testimony would be available for study as a possible basis for action during the next session." The Ways and Means Committee, he added has "an extremely heavy schedule and only a very limited time to devote to these hearings."

Other subjects listed for consideration are grants to states for old-age assistance; various aspects of Old Age, Survivors, and Disability Insurance; lowering retirement ages and new disability benefits; aid to dependent children, the blind, and the totally disabled; maternal and child welfare; and a review of the actuarial status of the OASI and Disability Trust Funds.

Testimony also may be heard on amendments to extend unemployment insurance coverage to employers of one or more persons and to bring physicians under social security.

CONGRESSIONAL DISTRICT POLL OPPOSES FORAND BILL

A congressman from Chicago has polled his district on a variety of subjects, including social security. In a newsletter to his constituents, Republican Rep. Harold L. Collier reports that on the question of whether the federal government should "embark upon a program to start financing medical care of all those under social security," 73% responded in the negative, 26% in the affirmative, and only 1% with no opinion.

Some other responses: Should mandatory social security be expanded? 47%, yes; 48%, no; 5%, no opinion. Do you favor proposals for a system of federal, national universities? 16%, yes; 81%, no; 3%, no opinion. To meet the need for scientists, do you favor government scholarships for higher education or some method such as tax benefits for business and individuals to finance expanded education? 26% favored federal scholarships; 68%, tax mechanisms, and 6%, no opinion.

DR. McGUINNESS ON MEDICAL RESEARCH, COST OF EDUCATION

The special health assistant to Secretary Folsom addressed a medical school graduating class this month and made some predictions and a few warnings. Dr. Aims C. McGuinness, talking to University of Texas–Medical Branch graduates, had this to say:

Medical Research–There is no question that medical research, estimated at a rate of 330 million dollars a year, must go forward at even higher levels of expenditure. This includes further expansion of facilities for teaching research personnel and expansion of research laboratories. "There is little question that the dollars will be available to carry on a steadily expanding program of medical research. But will adequate numbers of well-trained people like yourselves be available . . . to conduct this search for new knowledge and to bring it to the patients who need it when it becomes available?"

Medical School Construction Grants—"Unless our society acts quickly to increase greatly its investment in medical education, we will be desperately short of physicians, technologists, and research scientists, and we will fail to grasp a large part of the opportunity we now have for the improvement of the health of the American people."

Aging Problems—It is the urgent obligation of the medical and allied professions, the Blue Cross and Blue Shield, the insurance companies, government, and the people who use health services to join in an effort to extend voluntary health insurance to those who are not now protected and to broaden the types of coverage available. He said it was heartening to read the announcement of the formation of the Joint Council to Improve the Health Care of the Aged, which is working in this field.

Medical Care Costs—There is an urgent necessity for making every effort to hold the cost of medical care for the individual to the minimum by more sharply tailoring medical care to the individual's particular needs. "The decisions about who receives what kinds of medical care and where they receive it properly rest with physicians. Yet physicians sometimes tend to forget that they too have a responsibility in relation to the financial mechanism that is the essential underpinning to medical care today. . . . For doctors to increase their charges just because the patient has insurance defeats the purpose of prepayment."

MISCELLANY

Walter W. McDonald of St. Ignatius, Mont., has been named to the Public Health Service advisory committee on Indian health. The appointment, beginning July 1, is for four years. Mr. McDonald is a member of the Flathead Indian tribe and chairman of a confederated tribal council.

Federal loans to build housing for student nurses have been made to St. Mary's hospital, Amsterdam, N. Y.; Beth Israel Hospital Association, New York City; and Emanuel Hospital School of Nursing, Portland, Ore.

The American Red Cross is shipping Salk vaccine, cortisone, and gamma globulin to Poland for the relief of flood victims, in response to an appeal from the Polish Red Cross. The inventory is 1,250 vials of Salk vaccine; 45,000 cortisone tablets; 750 10-cc. and 500 20-cc. vials of liquid cortisone; and 28,000 cc. of gamma globulin.

CORRECTION

Medicare.—Through a transcribing error, quotations of Dr. F. J. L. Blasingame, A. M. A. General Manager, and Kenneth Williamson, director of the American Hospital Association's Washington office, were transposed in THE JOURNAL of May 17. The error occurred in an article on Medicare.

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Lown, B., and Levine, S. A.:
Current Concepts in Digitalis Therapy, Boston,
Little, Brown & Company, 1954, p. 23, par. 2.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.
1958 Annual Meeting, San Francisco, June 23-27.
1958 Clinical Meeting, Minneapolis, Dec. 2-5.
1959 Annual Meeting, Atlantic City, June 8-12.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.

AMERICAN

June

AMERICAN ACADEMY OF TUBERCULOSIS PHYSICIANS, San Francisco, June 21. Dr. Oscar S. Levin, P. O. Box 7011, Denver 6, Secretary.

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS, Claridge Hotel, Atlantic City, N. J., June 15-18. Dr. Leon Roizin, 722 W. 168th St., New York 32, Secretary.

AMERICAN COLLEGE OF ANGIOLOGY, Fairmont Hotel, San Francisco, June 21-22. Dr. Alfred Halpern, 15 E. 62d St., New York 21, Executive Secretary.

AMERICAN COLLEGE OF CHEST PHYSICIANS, Fairmont Hotel, San Francisco, June 18-22. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

AMERICAN DIABETES ASSOCIATION, Mark Hopkins Hotel, San Francisco, June 21-22. Dr. Franklin B. Peck Sr., 1 E. 45th St., New York 17, Secretary.

AMERICAN GERIATRICS SOCIETY, Mark Hopkins Hotel, San Francisco, June 18-19. Dr. Richard J. Kraemer, 2907 Post Road, Warwick, R. I., Secretary.

AMERICAN GOITER ASSOCIATION, St. Francis Hotel, San Francisco, June 17-19. Dr. John C. McClintock, 149½ Washington Ave., Albany, N. Y., Secretary.

AMERICAN MEDICAL ASSOCIATION, Sheraton-Palace Hotel, San Francisco, June 23-27. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

AMERICAN MEDICAL WOMEN'S ASSOCIATION, INC., San Francisco, June 19-22. Miss Lillian T. Majally, 1790 Broadway, New York 19, Executive Secretary.

AMERICAN NEUROLOGICAL ASSOCIATION, Claridge Hotel, Atlantic City, N. J., June 16-18. Dr. Charles Rupp, 133 S. 36th St., Philadelphia 4, Secretary.

AMERICAN PROCTOLOGIC SOCIETY, Los Angeles Statler, Los Angeles, June 29-July 3. Mr. Norman D. Nigro, 10 Peterboro St., Detroit 1, Executive Secretary.

AMERICAN RHEUMATISM ASSOCIATION, San Francisco, June 20-21. Dr. Edward F. Hartung, 580 Park Ave., New York 21, Secretary.

AMERICAN THERAPEUTIC SOCIETY, Mark Hopkins Hotel, San Francisco, June 19-22. Dr. Oscar B. Hunter Jr., 915 19th St., N. W., Washington 6, D. C., Secretary.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, Fairmont Hotel, San Francisco, June 23-27. Dr. Lorand V. Johnson, 10515 Carnegie Ave., Cleveland 6, Secretary.

CATHOLIC HOSPITAL ASSOCIATION OF THE UNITED STATES AND CANADA, Atlantic City, N. J., June 23-26. Mr. M. R. Kneifl, 1438 S. Grand Blvd., St. Louis 4, Mo., Executive Secretary.

MAINE MEDICAL ASSOCIATION, The Samoset, Rockland, June 22-24. Dr. Esther M. Kennard, P. O. Box 240, Brunswick, Secretary.

NATIONAL MEDICAL VETERANS SOCIETY, San Francisco, June 21-22. Dr. Henry C. Beekley, 3117 Warsaw Ave., Cincinnati, Secretary.

NORTH AMERICAN CHAPTER OF THE INTERNATIONAL CARDIOVASCULAR SOCIETY, Sir Francis Drake Hotel, San Francisco, June 21. Dr. Henry Haimovici, 105 E. 90th St., New York 28, Secretary.

SOCIETY FOR INVESTIGATIVE DERMATOLOGY, Clift Hotel, San Francisco, June 21-22. Dr. Herman Beerman, 255 S. 17th St., Philadelphia 3, Secretary.

SOCIETY OF NUCLEAR MEDICINE, Beverly Hilton Hotel, Los Angeles, June 19-21. Dr. Robert W. Lackey, 452 Metropolitan Bldg., Denver, Secretary.

THE ENDOCTRINE SOCIETY, St. Francis Hotel, San Francisco, June 19-21. Dr. Henry H. Turner, 1200 N. Walker St., Oklahoma City 3, Okla., Secretary.

WOMAN'S AUXILIARY TO THE AMERICAN MEDICAL ASSOCIATION, San Francisco, June 23-27. Miss Margaret Wolfe, 535 N. Dearborn St., Chicago 10, Secretary.

July

AMERICAN COLLEGE OF SURGEONS, SECTIONAL MEETING, Concert Hall, Stockholm, Sweden, July 2-7. Dr. Michael L. Mason, 40 E. Erie St., Chicago 11, Chairman.

AMERICAN SOCIETY OF FACIAL PLASTIC SURGERY, New York, July 16. Dr. Samuel M. Bloom, 123 E. 83d St., New York 28, Secretary.

IDAHO STATE MEDICAL ASSOCIATION, Sun Valley, July 6-9. Mr. Armand L. Bird, 364 Sonna Bldg., Boise, Executive Secretary.

INTERMOUNTAIN PEDIATRIC SOCIETY, Sun Valley, Ida., July 4-6. Dr. Thales H. Smith, 220 N. University Ave., Provo, Utah, Secretary.

ROCKY MOUNTAIN CANCER CONFERENCE, Shirley-Savoy Hotel, Denver, July 9-10. Alexis E. Lubchenco, 835 Republic Bldg., Denver 2, Chairman.

UNITED STATES SECTION, INTERNATIONAL COLLEGE OF SURGEONS, EASTERN REGIONAL MEETING, Manchester, Vt., July 1-5. Dr. M. Leopold Brodny, 636 Beacon St., Boston, General Chairman.

August

AMERICAN CONGRESS OF PHYSICAL MEDICINE AND REHABILITATION, Philadelphia, Bellevue-Stratford Hotel, Aug. 24-29. Dr. Frances Baker, 1 Tilton Ave., San Mateo, Calif., Secretary.

AMERICAN HOSPITAL ASSOCIATION, Palmer House, Chicago, Aug. 18-21. Dr. Edwin L. Crosby, 18 E. Division St., Chicago 10, Director.

AMERICAN VETERINARY MEDICAL ASSOCIATION, Sheraton Hotel, Philadelphia, Aug. 18-21. Dr. J. G. Hardenbergh, 600 S. Michigan Blvd., Chicago 5, Executive Secretary.

BIOLOGICAL PHOTOGRAPHIC ASSOCIATION, Shoreham Hotel, Washington, D. C., Aug. 19-22. Miss Jane Waters, Box 1668, Grand Central P. O., New York 17, Secretary.

CHEMICAL ORGANIZATION OF CELLS, NORMAL AND ABNORMAL, Madison, Wis., Aug. 21-23. Dr. J. F. A. McManus, Univ. of Alabama Medical Center, Birmingham, Ala., Chairman.

INTERNATIONAL COLLEGE OF SURGEONS, REGIONAL MEETING, WESTERN SECTION, The Riverside Hotel, Reno, Nev., Aug. 21-23. For information address: Dr. Leo D. Nannini, 190 Mill St., Reno, Nev.

NATIONAL MEDICAL ASSOCIATION, Hotel Schroeder, Milwaukee, Aug. 11-14. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

NORTHWEST PROCTOLOGIC SOCIETY, Sun Valley, Ida., Aug. 27-29. Dr. John McKay, 645 Medical Dental Bldg., Seattle, Secretary.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY, Shirley-Savoy Hotel, Denver, Aug. 15-17. Dr. John H. Freed, Denver 20, Secretary.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, The Greenbrier, White Sulphur Springs, Aug. 21-23. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

WORLD MEDICAL ASSOCIATION, Copenhagen, Denmark, Aug. 15-20. Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, Secretary-General.

September

AMERICAN ACADEMY FOR CEREBRAL PALSY, Sheraton-Biltmore Hotel, Providence, R. I., Sept. 25-27. Dr. Raymond R. Rembolt, University Hospitals, Iowa City, Ia., Secretary.

AMERICAN ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS, The Homestead, Hot Springs, Va., Sept. 4-6. Dr. E. Stewart Taylor, 4200 E. 9th Ave., Denver 20, Secretary.

AMERICAN COLLEGE OF PHYSICIANS, Mid-West Regional Meeting, Milwaukee, Wis., Sept. 27. Dr. James F. Gleason, 7 S. Oxford Ave., Atlantic City, N. J., General Chairman.

AMERICAN FRACTURE ASSOCIATION, Skirvin Hotel, Oklahoma City, Okla., Sept. 29-Oct. 4. Dr. H. W. Wellmerling, 610 Griesheim Bldg., Bloomington, Ill., Secretary.

AMERICAN MEDICAL WRITERS' ASSOCIATION, Hotel Morrison, Chicago, Sept. 26-27. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

AMERICAN ROENTGEN RAY SOCIETY, Shoreham Hotel, Washington, D. C., Sept. 27-Oct. 3. Dr. C. Allen Good, 200, 1st St. S. W., Rochester, Minn., Secretary.

COLORADO STATE MEDICAL SOCIETY, Broadmoor Hotel, Colorado Springs, Sept. 24-27. Mr. Harvey T. Sethman, 1612 Tremont Place, Denver 2, Executive Secretary.

KANSAS CITY SOUTHWEST CLINICAL SOCIETY, Municipal Auditorium, Kansas City, Mo., Sept. 22-25. Mr. A. L. Bingham, 3036 Gillham Rd., Kansas City 8, Mo., Executive Secretary.

KENTUCKY STATE MEDICAL ASSOCIATION, Brown Hotel, Louisville, Sept. 23-25. Mr. J. P. Sanford, 1169 Eastern Parkway, Louisville 17, Executive Secretary.

MICHIGAN STATE MEDICAL SOCIETY, Sheraton-Cadillac Hotel, Detroit, Sept. 30-Oct. 3. Dr. L. Fernald Foster, 606 Townsend St., P. O. Box 539, Lansing, Mich., Secretary.

MISSISSIPPI VALLEY MEDICAL SOCIETY, Morrison Hotel, Chicago, Sept. 24-26. Dr. Harold Swanberg, 510 Main St., Quincy, Ill., Secretary.

MONTANA MEDICAL ASSOCIATION, Northern Hotel, Billings, Sept. 11-13. Mr. L. R. Hegland, P. O. Box 1692, Billings, Executive Secretary.

NEVADA STATE MEDICAL ASSOCIATION, Elko, Sept. 17-20. Mr. Nelson B. Neff, P. O. Box 188, Reno, Executive Secretary.

NEW HAMPSHIRE MEDICAL SOCIETY, Mt. Washington Hotel, Bretton Woods, Sept. 19-22. Mr. Hamilton S. Putnam, 18 School St., Concord, Executive Secretary.

NORTHEASTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Equinox House, Manchester, Vt., Sept. 12-13. Dr. F. O. Harbach, 831 James St., Syracuse, N. Y., Secretary.

OREGON STATE MEDICAL SOCIETY, Columbia Athletic Club, Portland, Sept. 3-5. Dr. Max H. Parrott, 1020 S. W. Taylor St., Portland 5, Secretary.

TEXAS ACADEMY OF GENERAL PRACTICE, San Antonio, Tex., Sept. 22-24. Mr. Donald C. Jackson, 1905 N. Lamar, Austin, Tex., Executive Secretary.

TRI-STATE MEDICAL SOCIETY, Shreveport, La., Sept. 18. Dr. J. C. Sanders, Sanders Clinic, Kings Highway, Shreveport, La., Secretary.

UNITED STATES SECTION, INTERNATIONAL COLLEGE OF SURGEONS, Atlantic City, N. J., Sept. 7-11. Dr. Karl Meyer, 1835 W. Harrison, Chicago, Secretary.

UTAH STATE MEDICAL ASSOCIATION, Hotel Utah, Salt Lake City, Sept. 9-12. Mr. Harold Bowman, 42 S. Fifth East St., Salt Lake City 2, Executive Secretary.

VERMONT STATE MEDICAL SOCIETY, Mt. Washington Hotel, Bretton Woods, N. H., Sept. 20-22. Mr. Getty Page, 128 Merchants Row, Rutland, Vt., Executive Secretary.

WASHINGTON STATE MEDICAL ASSOCIATION, Davenport Hotel, Spokane, Sept. 14-17. Mr. Ralph W. Neill, 1309 7th Ave., Seattle, Executive Secretary.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, Palmer House, Chicago, Oct. 12-17. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Palmer House, Chicago, Oct. 20-23. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill., Executive Secretary.

AMERICAN ASSOCIATION OF MEDICAL CLINICS, Palace Hotel, San Francisco, Oct. 2-4. Dr. John R. Hand, 1216 Southwest Yamhill St., Portland, Ore., Secretary.

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PRECAUTIONS IN USE OF ANTIHYPERTENSIVE DRUGS, INCLUDING CHLOROTHIAZIDE

Robert W. Wilkins, M.D., Boston

The aim in antihypertensive therapy should be to lower the blood pressure gradually by using the safest, mildest, and least symptom-producing drugs; dosages are determined by patient observation over weeks or months of time. One of the various preparations of Rauwolfia should be used first, an effort being made to achieve the antihypertensive effect without depression. A second drug, Veratrum, may be added if extensive trial has shown the first alone to be inadequate. Again an effort is made to lower the blood pressure without side-effects; in the case of Veratrum these are usually nausea and vomiting, rarely cardiac arrhythmia and collapse. A third drug to be tried with Rauwolfia is hydralazine; it is a potent hypotensive drug, but it can have acute and chronic toxic effects. The fourth is chlorothiazide, which can, in addition to a desirable hypotensive effect, cause diuresis and quickly deplete the body of potassium. The dosage should be kept low and supplements of potassium should be given in patients receiving long-term treatment. A fifth class of available drugs are the ganglionic blocking agents, the dosages of which are so critical that especially exacting care is needed in adapting them to the individual case. Each class of drug may be used in combination with the others, but every change should be instituted gradually. By use of minimal effective doses of drugs in combination, a safe antihypertensive regimen can generally be developed.

Powerful tools can be helpful or dangerous, depending on how they are used. This is particularly true of drugs. An agent that is capable of suddenly altering a vital physiological function such as blood pressure may be either lifesaving or lethal depending on when and how it is given. As more effective hypotensive drugs become available, increasing caution is required in regulating the timing and sizing of their doses, particularly if they are to be used in combination. Conservatism as to the size of doses and the rate of change of doses is one key to success, especially if therapy is to be continued over long periods of time, as usually is required in the management of essential or primary hypertension. This is particularly true in patients past middle age, who do not easily tolerate sudden shifts in their fundamental physiological functions.

Selection of Drugs

Unless there is great urgency for an immediate striking hypotensive effect, as there may be in cases of hypertensive encephalopathy or "malignant" retinopathy, the aim in antihypertensive therapy should be to lower blood pressure gradually through the use of the safest, mildest, and least symptom-producing agents and doses. This obviously requires a process of trial and error in each patient over weeks or months of time. In the usual case of gradually progressive or nonprogressive hypertension there is ample time to undertake such a trial. Although there is a rough correlation between the amount of treatment necessary and the severity of the disease (as indicated by height and "fixation" of the diastolic pressure, the prior duration of the disease, and the extent of vascular complications in the eyegrounds, brain, heart, and kidneys), the proper selection of

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From the Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

drugs and dosages can be determined only by trying them in a given patient. Therefore therapy is always begun with the mildest drug, Rauwolfia, which may be surprisingly efficacious, even when given alone and in severe cases.

The next drug to be added to Rauwolfia, if necessary, is Veratrum. Veratrum is a powerful hypotensive agent, but it has a built-in limiting or safety feature in its emetic action which serves to protect the individual from lethal doses of the drug given by mouth. After over 10 years experience with this agent, I am confident that it is relatively safe; for even when collapse reactions occur from overdosages, they are rarely if ever fatal. Certainly slow accumulation or chronic toxicity does not occur from Veratrum.

The third drug to be added (or the second if pulse rate is already low on Rauwolfia without Veratrum) is hydralazine. Hydralazine is a potent hypotensive drug, but it can have acute and chronic toxic effects. These may be in the nature of individual idiosyncrasy but are usually related directly to the size of the doses taken. Fourth on the list of hypotensive drugs is chlorothiazide, the new orally effective, synthetic diuretic. This drug has powerful effects on electrolyte excretion and can quickly deplete the body of potassium. Doses necessary for a desirable hypotensive effect over prolonged periods of time can and should be kept low, as compared with those necessary to control edematous states.

The last group of hypotensive drugs to be employed are the ganglionic blocking agents. Dosage is so critical with these drugs that the term "titration" is employed to indicate the exacting care that is necessary in the individual regulation of doses. The purpose of this paper is to point out the precautions to be used in giving each of these drugs, and the unfortunate results that may happen when these precautions are ignored.

Rauwolfia and Reserpine

Details as to various commercial preparations of Rauwolfia and their dosages were given in a recent publication.[1] It was pointed out there that reserpine seems to be the chief active hypotensive principle as well as the chief "tranquilizing" principle in this drug. (Whether these two principles are really separable is open to question.) Because reserpine is used freely in large dosages and with relative safety in psychiatric cases, doctors have been inclined to employ what to me seem unnecessarily large doses in the chronic treatment of hypertension.

While initial dosages of reserpine up to 1 mg. a day may be more rapidly effective in lowering blood pressure (as indeed 5 mg. parenterally may be in cases of encephalopathy) there is little if anything to be gained by continuing such doses beyond a few days. My initial dosage of reserpine in a new ambulatory patient rarely exceeds 0.4 mg. a day (given in four 0.1-mg. doses), whereas the continuing dosage after a few weeks or months of therapy rarely exceeds 0.2 mg., and often is only 0.1 mg. a day. Undoubtedly this low dosage schedule accounts for the rarity with which I have encountered mental depression and for the fact that I have never had a suicide of a patient taking Rauwolfia in any form. However, I believe that my results in hypertension compare favorably with those of physicians who routinely employ doses of Rauwolfia up to 10 times larger than I do.

As just indicated, the duration of continuous treatment with Rauwolfia is most important in determining the amount of the drug that can be safely tolerated. I have had many patients who after even one to two years have had to have their doses of Rauwolfia further reduced, because of the development of intolerable sedation or depression. For example, a few such patients can tolerate no more than 0.1 mg., and an occasional one no more than 0.05 mg., of reserpine a day. As a rule the hypotensive effect can be maintained by giving doses of the drug just below those causing intolerable sedation.

Whether anything is to be gained by using one form or preparation of Rauwolfia in preference to another remains unsettled. Rauwolfia in any form has such a slow gradual action that to sharply assay its clinical effects is most difficult. This applies equally to its hypotensive and to its "tranquilizing" effects. Therefore when one undertakes to make exact comparisons of these two effects among several different preparations of the drug, i. e., to determine their "hypotensive-sedative ratios," one has embarked on an arduous task.

I suspect that my experience with Rauwolfia would be considered "extensive" if the variety as well as the number and duration of my clinical trials were considered. Be that as it may, I have found that in treating hypertensive cases clinically there is little to choose between using crude Rauwolfia, the alseroxylon fraction, or reserpine,[1] provided one employs doses of each low enough to avoid untoward side-effects, particularly depression. In many patients these doses decrease markedly with time and often are as low as 0.1 mg. of reserpine, 2 mg. of alseroxylon, or 50 mg. of crude root a day.

However one practical difficulty still exists, which at first may seem trivial. That has to do with the size of pills that are available. Tablets containing more than 100 mg. of the crude root are not usually made because the bulk of the drug is so large. However it just so happens that this size tablet of crude drug suffices quite well since the drug in this dose is effective when given one to four times a day. As best I can judge, an equivalent dose (hypotensively and sedatively) of reserpine is somewhere near 1/1,000th (by weight) of the effective dose of the crude root in the same patient. But the usual pills of reserpine contain 0.25 mg. (1/400th the weight of the usual crude pill) and therefore in my opinion would represent considerably more, certainly not less, activity than a 100-mg. tablet of the root. Hence the tendency of the practitioner to overdose with reserpine as compared with crude root.

As for alseroxylon, I estimate that it represents in activity the equivalent of about 50 times the weight of crude root and about 1/20th the weight of reserpine. Fortunately, the manufacturers have made the tablet size of alseroxylon (2 mg.) roughly equivalent to that of the 100-mg. tablet of crude root and definitely less than that of the 0.25-mg. tablet of reserpine. Put another way, a 0.25-mg. tablet of reserpine would be equivalent to at least two tablets of alseroxylon or crude Rauwolfia.

The point is that, because of the sizing of the pills made generally available by the manufacturers, total daily doses of 1 mg. (or more) of reserpine are commonly recommended and used, whereas total daily doses of 20 mg. of alseroxylon, and especially of 1 Gm. of crude Rauwolfia, are rarely if ever suggested for the treatment of hypertension. If my estimations of the relative potencies of these preparations are even approximately correct (and I have good reason to believe they are), I would only expect that reserpine would be blamed (as it is) by clinicians for being more "toxic" than the less purified forms of the drug.

In addition to depression, side-effects of Rauwolfia which may require a reduction in dosage include first of all nasal stuffiness. This appears to be due to vascular congestion of the turbinates, and it may be associated with easy nasal bleeding, or with acute or chronic sinusitis. Vasoconstrictive nasal drops or inhalations often adequately offset this unpleasant side-effect, and occasionally an antihistaminic agent may relieve it. Weight gain frequently, insomnia or diarrhea occasionally, and bradycardia rarely are great enough to necessitate a reduction in dosage of Rauwolfia.

Veratrum

Although pure alkaloids and purified extracts of Veratrum are available, for practical purposes they all have the same objectionable feature as the crude drug, namely that they readily cause nausea and vomiting. From the doctor's point of view this feature may not be undesirable, since it makes overdosing with the drug so unpleasant that patients are not likely to do this very often. Nevertheless, collapse can occur on excessive dosage, and, in association with it, cardiac arrhythmias as well as vomiting may appear. The chief undesirable characteristic of such an overdosage effect is that it may occur with very little increase in the dosage over that necessary to produce a desirable hypotensive effect. Therefore in order to get the maximal beneficial action from Veratrum a patient must be always uncomfortably close to nausea.

These critical dosage characteristics make it necessary to be very precise with the timing of doses during the administration of Veratrum. Patients are advised to take the drug by the clock, e. g., with meals and at bedtime, and never oftener than every four hours. The first dose in the morning (after fasting) may be larger than the noon or supper doses, as may be the bedtime dose (since lying in bed lessens the tendency to nausea or collapse). Thus a common Veratrum schedule, using the alkavervir fraction (Veriloid), is, at breakfast 3 mg.; lunch 1.5 mg.; supper 1.5 mg.; and at bedtime 3 mg.

Given in association with Rauwolfia (e. g., Rauwiloid + Veriloid), even larger doses of Veratrum may be tolerated, as for example, 1 tablet (3 mg.) four times a day, or 1½, 1, 1, 1½ tablets in the four doses respectively. (Incidentally, this latter dosage provides a total of 5 mg. of alseroxylon.) A word as to the use of such combined pills. The purist may rightly object to combination tablets, but patients as a rule greatly prefer taking one tablet to two separate ones. Indeed many apprehensive patients bridle at taking a dosage of two separate tablets at a time, even of the same kind, because they interpret this as meaning that they are more seriously ill. My experience has been that patients have fewer lapses and make fewer mistakes in dosage, the simpler the regimen can be made. Therefore I do not hesitate to use more than one medicament combined in one tablet, provided this gives approximately the correct dosage of each.

The best compromise with Veratrum in any case is for the patient and the physician to become familiar with a single standardized preparation of the drug and gradually to change the dose as necessary to get the best clinical effect with the least nausea. Epigastric, substernal, or pharyngeal burning with salivation often precede nausea and may be useful premonitory symptoms of overdosage. If the patient will lie down at the appearance of these symptoms and omit or reduce the next dose (and then slightly reduce the same dose the next day), he may prevent a recurrence of these overdosage effects.

Hydralazine

Hydralazine is a potent and useful hypotensive drug, but success in its use is dependent mostly upon the manner in which it is given. Indeed, after my first trials with this drug I discarded it because the side-effects seemed too difficult to manage. However by giving preliminary or simultaneous doses of Rauwolfia and by using smaller initial doses of hydralazine, its side-effects were so minimized that my unfavorable opinion was completely altered.

Rauwolfia or reserpine greatly lessens a patient's initial reactivity to hydralazine which usually causes more or less occipital headache and palpitation (possibly due to histamine release). By starting with doses of only 10, or even 5 mg., four times a day and gradually increasing these amounts, one can make the drug tolerable to most patients even in the usual necessary dose of 50 mg. four times a day. However in many patients a total dose of only 100 mg. (25 mg. four times a day) given in combination with reserpine 0.2 or 0.4 mg. a day may suffice to restore the blood pressure to the desired level. The highest dosage of hydralazine I ever use now is 400 mg. a day, and this only upon cautiously demonstrating that it is both well tolerated and efficacious in lowering blood pressure.

Hydralazine, presumably by stimulating cardiac output, can cause angina pectoris in patients with otherwise asymptomatic coronary disease. This manifests itself as substernal aching which is not as clearly related to effort or excitement as in the typical case of angina but often is associated with electrocardiographic changes suggesting myocardial anoxia. While a downward adjustment of the dosage of hydralazine may relieve this side-effect, it would seem preferable to omit the drug altogether in any patient who develops angina while taking it. However it is only fair to say that I know of no deaths from coronary disease in which hydralazine has been clearly implicated.

At the first sign of a hypersensitivity reaction either in the skin, joints, or blood (lupus erythematosus cells, or anemia) hydralazine therapy is stopped. On the relatively low dosages now recommended such complications are rare.

Chlorothiazide

Chlorothiazide, a new orally effective diuretic, is particularly useful as an adjunct with other antihypertensive treatment, whether drugs or splanchnicectomy.[1] The rationale for its use is based on three considerations: 1. Experimentally, almost every procedure that tends to lower blood pressure also tends to cause antidiuresis and sodium retention, which presumably are part of the homeostatic mechanisms that maintain blood pressure.[2] 2. Clinically, hypotensive drugs, particularly Rauwolfia and hydralazine, may cause fluid retention, even to the extent of producing dependent edema. 3. Hypotensive procedures may lose their effectiveness when there is a subclinical, but especially when there is a clinical, retention of sodium and water, particularly with congestive heart failure. Diuresis may then restore the effectiveness of the hypotensive procedure.

Chlorothiazide is tolerated by most patients over long periods of time if given in moderate daily doses. It is a very potent diuretic, being about as effective orally as mercurial preparations are parenterally. It has no serious toxic effects, at least so far as is now known, although a few instances of skin rash have been noted among patients taking this drug. Nevertheless, chlorothiazide can have some untoward side-effects which necessitate caution in its use, particularly when given continuously for long periods of time.

A lowering of the serum potassium level occurs in roughly 40% of patients taking chlorothiazide continuously without supplementary potassium for more than a week. In half of these cases the serum potassium level may be reduced below the lower limit of normal (3.5 mEq. per liter). Apparently the body itself in time may correct or lessen the hypokalemia (as it does the hyponatremia) without special dietary supplements of potassium. Restriction of dietary sodium apparently increases the likelihood of hypokalemia, presumably because the kidney will excrete potassium more actively if sodium is not freely available. Therefore patients starting on chlorothiazide should not be placed on a low-sodium diet, and patients already on a low-sodium diet should relax it when chlorothiazide therapy is instituted. Even with this precaution serum potassium level may become so low that it is alarming to the physician and I suspect may be harmful to the patient, especially if he is subject to cardiac arrhythmias as a result of digitalization, coronary ischemia, or both.

For these reasons I never prescribe chlorothiazide for a new patient who may have coronary disease or who is taking digitalis without instituting the chlorothiazide therapy most cautiously and supplementing the intake of potassium as indicated by weekly determinations of the serum potassium level as well as by clinical and electrocardiographic assessments of myocardial irritability and digitalis intoxication. Potassium may be given either in a solution (potassium Triplex) or with specially coated or prepared tablets of potassium chloride. Routinely 14 mEq. of potassium (1 Gm. of potassium chloride) is prescribed in such cases two to four times a day, unless there is renal insufficiency, in which case measurements of the serum potassium level must be utilized to determine the need (if any) for supplemental potassium.

There have been five deaths among several hundred patients who have been given chlorothiazide in this hospital. All these patients were known to have severe generalized vascular disease, had had prior coronary occlusions, or had complained of angina pectoris. Three patients had had a lumbothoracic splanchnicectomy at least 10 years previously. In two of the patients chlorothiazide therapy had been stopped several days prior to death. However, the deaths were "cardiac" in all and were sudden in all but one. Obviously in such critically ill patients sudden death is not unusual and could not be blamed with certainty on the medicament being taken.

Nevertheless it seems possible that there may have been a connection between the use of chlorothiazide and death in some of these cases. This is because in other patients chlorothiazide apparently has precipitated arrhythmias or has caused digitalis intoxication, presumably by producing a diuresis with or without hypokalemia. My present thinking is that patients with areas of myocardial ischemia due to coronary disease (with or without hypotension) may be particularly susceptible to hypokalemia, or to some change in sodium-potassium balance caused by chlorothiazide, which in them may cause a fatal arrhythmia such as ventricular fibrillation.

Chlorothiazide rarely if ever appears to aggravate or cause angina pectoris, as hydralazine may do, in patients with known coronary disease. Indeed it may give striking relief to certain patients with the anginal syndrome, especially if an important component of their discomfort is shortness of breath on exertion. Many anginal patients prefer chlorothiazide to nitrites for prevention of their attacks. For these reasons, when antihypertensive treatment in addition to Rauwolfia and Veratrum appears to be urgently needed in a patient with known or suspected coronary disease, with or without angina pectoris, I am inclined to try chlorothiazide before using hydralazine. However, all the precautions already mentioned in connection with such cases are routinely followed.

As to dosage, chlorothiazide should be given in hypertension in the minimal dose effective in reducing the blood pressure to the desired level. To a large extent this dose will be determined by the treatment being continued at the time of the institution of chlorothiazide. Unless the patient has undergone splanchnicectomy or is taking a ganglionic blocking agent, a starting dose of 125 mg. (½ tablet) twice a day is safe and adequate for initial trial in most patients. However patients with surgically removed or chemically blocked sympathetic nervous systems may be exquisitely sensitive to the hypotensive effect of chlorothiazide and require an extremely cautious approach in their use of this drug. Thus, initially only 62.5 mg. once or twice a day should be given to such patients, and care should be taken to reduce drastically the doses of any ganglionic blocking agent being used, if and as the chlorothiazide is increased. Otherwise severe postural hypotension and collapse may occur.

If, after a week or two at a low-dosage level, blood pressure is still elevated and the serum potassium level is normal (with or without supplementary dietary potassium), the dosage may be raised (with supplementary potassium), if and as necessary, to 250 mg. three or even four times a day. My usual maximum dosage of chlorothiazide for hypertension therefore is 750 mg. to 1 Gm. a day. This is considerably smaller than the doses usually advocated, especially for congestive failure. An additional point is that by dividing the total daily dose into four separate parts apparently a better hypotensive (and diuretic) effect may be achieved with less drug than by giving the total dose all at once. Presumably this is because the kidney rapidly excretes chlorothiazide below the level of its maximal therapeutic effect. In nonedematous patients, there is no reason for not giving a dose at bedtime, since nocturia does not occur on continued therapy (except perhaps initially). Actually, nocturia may be relieved by giving chlorothiazide in the daytime, apparently because, by producing diurnal diuresis, the drug restores the normal pattern of nocturnal antidiuresis.

Conservative doses also help prevent other less frequent but disturbing side-effects of chlorothiazide. These include hyponatremia, hypochloremic alkalosis, weakness and trembling (related in part to hypokalemia), elevation of the serum nitrogen level, sexual impotence, and nausea and epigastric discomfort. In addition, for chronic continuous therapy I see no benefit in using larger doses of this drug when the addition of some other symptomless agent to the regimen may suffice to restore the blood pressure to the desired level. It is well to remember that chlorothiazide has been used continuously for only one year, and as yet we do not know whether true toxic reactions, sensitivity, or other unfavorable side-reactions may occur only after a longer period of use. It seems prudent therefore to reserve this drug for third or fourth place in the usual trial of hypotensive agents.

Ganglionic Blocking Agents

Starting doses of the many available preparations of ganglionic blocking drugs should be low.[1] They should be added cautiously to a combined regimen of drugs such as those already mentioned only if this regimen already is being given in maximal tolerable dosages and without adequate results. Since ganglionic blocking agents cause postural hypotension, their effects should be judged by taking blood pressure with the patient in the upright as well as in the sitting and recumbent positions. Indeed, the chief hazard from using these drugs is that the patient's blood pressure may collapse, particularly while he is standing, and, if he faints, may cause him to injure himself. In addition, if the patient has vascular disease he may suffer from signs and symptoms of cerebral or coronary insufficiency during such an episode, from which he may or may not have long-term residual effects, apparently depending on the severity and duration of the ischemia resulting from the collapse. Fortunately, serious vascular accidents are not common after the use of ganglionic blocking agents. Nevertheless they can occur, and this should be remembered whenever these drugs are being considered for a given patient. Every patient should be warned of the possibility of a collapse reaction, especially on standing, and should be cautioned to lie down if he feels weak or faint after taking a blocking agent and then to reduce his dosage of the drug.

As with other types of hypotensive drugs, familiarity with one or two preparations as to the dosages and actions in the particular patient under treatment is the most important factor in their successful use. In my hands pentolinium seems to be somewhat more effective in the average case than any other single ganglionic blocking agent. However it may not be tolerated by a given patient as well as some other preparation, or, rarely, it may appear to be quite inactive. In such an instance the use of chlorothiazide should be considered, if it is not already being used, since it may restore the patient's reactivity to the ganglionic blocking agent. If chlorothiazide is not effective and if the urgency to lower blood pressure remains great, another blocking agent may be tried. Pentolinium is initiated in a dose of 20 mg. and is increased by 10 mg. per dose (separated by at least six hours) until some postural hypotensive effect is achieved. At this point further increases in dosage are made very cautiously if and as necessary.

General Precautions

There are some general precautions that should be considered in the management of any patient under antihypertensive treatment.

1. Take time. Persistence is the first requirement for success.

2. Be gradual. Institute drugs and change doses gently. As a rule, sudden changes in blood pressure are not well tolerated by hypertensive patients, particularly elderly ones who may have vascular disease and are subject to vascular accidents.

3. Be satisfied with a reasonably satisfactory objective; do not demand a normal blood pressure in every case. A diastolic pressure of 100 mm. Hg or lower is usually adequate. This also is particularly true in elderly patients who may have had hypertension for years.

4. Be content with a given, reasonably satisfactory regimen. Do not switch over to every new drug that becomes available. Again this warning is particularly pertinent in elderly patients, especially with respect to the use of chlorothiazide and ganglionic blocking agents. If an elderly patient is doing well clinically, let his regimen alone, especially if his disease has not progressed for several years.

5. Use drugs in combination if necessary; do not be too much of a purist. Like it or not, antihypertensive drugs usually work better and with fewer side-effects when used in combination than when given singly. But do not use more drugs than necessary.

6. Hypotensive drugs, except for the ganglionic blocking agents and possibly chlorothiazide, tend to increase gastric secretion and may aggravate if not actually cause peptic ulcers. Antacids should be given to all patients known or suspected to have an ulcer, if they are to be treated with hypotensive drugs. Antacids might well be considered in every patient under such treatment.

7. Weight gain is particularly apt to occur in patients on therapy with Rauwolfia or reserpine. Since weight reduction is to be encouraged in overweight hypertensive patients and weight gain is to be prevented in all, patients should be encouraged to go on a low-fat diet (eliminating fats as far as practicable). This is a relatively easy way of counteracting the weight-gaining effect of Rauwolfia and, for what it is worth, may possibly help offset a tendency to hyperlipemia and atherosclerosis.

8. Reducing the dose of an offending drug is usually preferable to adding a counteracting drug. For example, it is usually better to reduce the dose of resperine than to add an "energizer" in cases of excessive sedation. Similarly, except for the use of laxatives to decrease constipation, it is better to reduce the dose of a ganglionic blocking agent than try to counteract all its side-effects with a parasympathomimetic agent. In this connection it is well to remember that chlorothiazide may lessen the necessary dosage of a blocking agent and in addition may have hypotensive effects of its own.

9. Other "vasodilating" or "hypotensive" influences such as hot weather, fever (as from infections), alcohol, dehydration (as from diarrhea), starvation, or a strict low-sodium diet may act additively with hypotensive drugs to lower blood pressure unduly. Patients should be warned to reduce their doses of drugs if they catch cold, or have the "flu," with or without diarrhea. The physician may wish to reduce their doses in the spring and summer but may wish to raise them again in the autumn. Alcohol should be used moderately if at all.

10. In time, with or without taking and recording his own blood pressure, an intelligent patient may become quite expert in managing his own antihypertensive regimen. It is well gradually to acquaint him with the actions and side-effects of each agent. However, he should be discouraged from making any sudden or drastic change in his regimen unless he finds himself in serious difficulty. A steady smooth course is desirable, and this can be attained only if the patient leads a smooth life and takes his medicaments steadily. The patient should be encouraged to tell the doctor "all"; in this way he and his physician learn how best to control his blood pressure with the least side-effects. A reasonable compromise, not perfection, is usually obtainable in most cases.

11. Continue to try to reduce dosages of drugs or omit them altogether if and as this can be done without an unfavorable effect. There is no question that "it is easier and requires less medication to keep a blood pressure down than to get it down." Even though later it may be necessary, especially

during stress or in cold weather, to resume a heavier schedule of drugs, reducing the dosage as much as possible undoubtedly is beneficial not only psychologically and physically but financially as well. The watchword in drug therapy is always to use the minimum that is effective.

Summary and Conclusions

Proceeding from the milder to the stronger antihypertensive drugs, one may try successively and in combination Rauwolfia, Veratrum, hydralazine, chlorothiazide, and a ganglionic blocking agent. By using minimal effective doses in combination, a safe and asymptomatic regimen can usually be found that will achieve a reasonable lowering of blood pressure. Dosages and changes in dosages should be instituted gradually. Repeated attempts should be made to reduce dosages or omit drugs altogether when this can be done without a rise in blood pressure. Caution should always be exercised, particularly with the stronger agents and with continued long-term therapy. How they are used is the most important single factor in the successful use of these agents. Each drug may be employed in combination with other therapy.

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RENAL RESPONSE TO EXERCISE—URINARY FINDINGS

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The albuminuria that frequently occurs in athletes after severe exercise has been observed not only in contact sports but also in sports like rowing, which are nontraumatic and certainly involve no body contact. This study concerns urinary findings after severe exertion at rowing, swimming, lacrosse, track, and football. The percentage of athletes having albumin, red blood cells, and casts in their urine after severe exercise was similar in all five sports. With respect to the finding of red blood cells, swimming, lacrosse, and track were about the same (80%), and football and rowing about even (55%). The 1,500-meter swimmers and the long distance track men showed the greatest amount of all three abnormal urinary findings. The duration of the event played a major part in determining the degree of the abnormality, and in the 1,500-meter race especially the urine was often loaded with red blood cells and casts. These usually disappeared within 24 hours, but the question is raised whether kidneys handicapped by previous infections can go through such experiences without cumulative damage.

Fifty years ago albuminuria, characterized as functional, was reported to occur in athletes after severe exercise.[1] A later study[2] found albumin, casts, and red blood cells in the urine of marathon runners and baseball players. Recently studies of football players[3] and boxers[4] have shown similar findings. These were all sports which carried with them some direct trauma to the kidneys such as jostling or shaking of the kidneys in marathon runners and direct blows in football and boxing contests. The football and boxing reports emphasized the red blood cells as a result of trauma. The report of Boone and associates[5] on hematuria in football players suggested to one of us (E. P. A.) that perhaps the red blood cells were not after all due to trauma as supposed, but to the response of the kidneys to the severe exercise itself. For that reason a rowing crew was studied and the findings reported.[6] Rowing is a sport which is truly nontraumatic to the kidneys, so that these findings were interpreted as being the result of the severe exercise alone.

Gardner,[7] reporting on athletic pseudonephritis, suggested that the urinary findings in football players are exactly the same as those in acute glomerulonephritis. The only way of distinguishing the two is the disappearance of these abnormal

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findings within a week after football scrimmage has been discontinued. It may then be assumed that this was not a nephritis. His figures on football players compare closely with those of Boone. Thus, in exercises where there is considerable body contact, such as football, boxing, horseback riding, or jeep riding over rough territory, there is actual trauma to the kidneys superimposed on the physiological changes due to the exercise alone. This type of exercise naturally may increase the amount of blood in the urine of injured players. But is the percentage of players with blood higher than in noncontact sports? Stimulated by the results of the experiments with the crew men, we have just completed a study of swimmers. This sport we also consider as being nontraumatic to the kidneys. Track and lacrosse were also investigated. The former may be questionable as to direct trauma, but certainly the latter is traumatic.

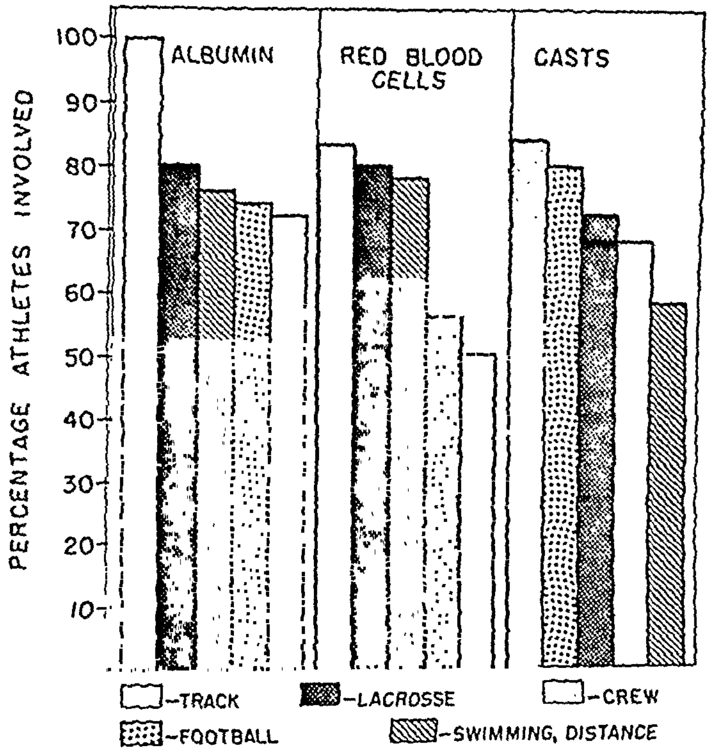


Fig. 1.—*Relative percentages of athletes showing urinary sediment after engaging in sports.*

In all of these sports the contests are intercollegiate matches in which the maximum amount of effort is put forth. Figure 1 is a summarized composite graph of the five sports. The striking thing is the similarity in urinary findings in all these sports. Between 60% and 80% of these athletes have albumin, red blood cells, and casts in their urine after severe exercise. It is also evident that there is not much difference in the percentage of athletes with red blood cells in their urine, whether the sport is renal traumatic or nontraumatic in character. Swimming, lacrosse, and track are about the same (80%) and football and crew about even (55%). However, participants in football and boxing often had red blood cells greater in numbers than those in the other sports, for some of them had gross hematuria. This we assume was due to direct renal trauma.

All of these specimens were examined by us personally and with considerable time and care. Perhaps this accounts for the finding of such a high percentage of red blood cells and casts in the urine. If careful search is made, it is not rare to find a faint trace of albumin and/or 1 to 2 red blood cells per high-power field in the urine of normal individuals. Hence these slight variations were not considered particularly abnormal. Gradations on the charts are made in the following manner: 1. Albumin: 0 to trace, considered none. Recordings were made according to 1+, 2+, 3+, and 4+ levels. 2. Red blood cells: 0 to 2 per high-power field in the centrifuge specimen was considered negative. Recordings of 3 to 5 per high-power field and then all over 6 per high-power field were made. 3. Casts: 0 to 2 per high-power field, considered negative; 3 to 5 per high-power field, and those over 6 per high-power field are charted. These urine specimens were collected immediately after the contest by us personally. The albumin and microscopic examinations on the centrifuged specimens were carried out by us at once.

Results

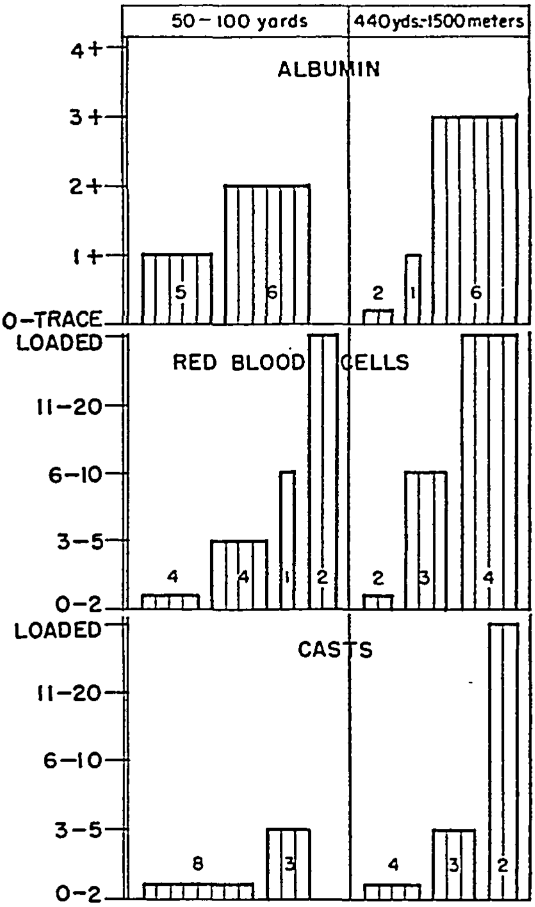
Figure 1 shows the relative percentages of the number of athletes engaging in lacrosse, football, rowing, track, and swimming. The striking over-all picture of this chart is that, in all sports, between 50% and 80% of the contestants showed albumin, casts, and red blood cells in the urine. Albumin was present in about equal percentages, between 70% and 80% of all sports, with the exception of long-distance track with 100% albuminuria. As to the red blood cells in the urine, the long-distance track, lacrosse, and swimming are grouped together at about 80%; football and crew had about 50%. One is perhaps surprised that not a higher percentage of football players had red blood cells in their urine, since it is a rough contact sport. But the variable factor which is significant in football is how long did the man play in the game and how much exertion did he really put forth. For instance, a player might get in a game for just a few minutes and not exert himself very much at that. He would probably not have the abnormal findings in the urine that a long-distance track man would who ran hard for two miles. The amount of energy put forth by these two individuals would be entirely different.

On the other hand the amount of actual blood in the urine, in many of the football players, was more than in the other sports. This was probably due to the addition of a contact trauma to the kidney itself. This would be true also in lacrosse. The fact that our lacrosse players have a higher percentage of red blood cells than football men similarly depends on the fact that the players in lacrosse were constantly active while in the game and there were few substitutions. These athletes played most of the game and had a much longer duration of active exercise than the football players. All the sports showed between 60% and 85% of the participants having casts in the urine. Generally, we can say that the urine which contained much albumin usually was loaded with casts and red blood cells. In a few instances, this was not necessarily so. Two or three had a lot of albumin, many casts, and only a few red blood cells. However, this finding was not the rule.

In figures 2, 3, and 4, each small column represents one athlete. At a glance one can tell how many men had that amount of albumin, red blood cells, or casts in the urine. Figure 2 shows the urinary findings in swimmers in intercollegiate contests. They are divided into the short events of 50 to 100 yards and the distance events of 440 yards and 1,500 meters. It is quite evident from a glance at these charts that the length or duration of the event plays a major part in the degree of the abnormal findings. For instance, in the 50-to-100-yard short swimming events, all of the swimmers had some albumin but it was only a little, and a good percentage of them had very few red blood cells and casts. In the distance events, the 440-yard and particularly the 1,500-meter race which calls for a tremendous amount of energy output, the number of athletes whose urine contains a 3+ albumin and is loaded with red blood cells and casts is very much higher.

The 1,500-meter swimmers and the long distance track men showed the greatest amount of all three abnormal findings in the urine. Of the nine long-distance swimmers examined, six of them had 3+ albumin, three of them had 6 to 10 red blood cells, and four were loaded with red blood cells: two of these were loaded with casts and three had 3 to 5 per high-power field. These were the outstandingly high quantitative abnormal findings in the urine of all the athletes. In contrast to this are the findings in 11 short-distance contestants. In the short-distance swimmers there were 3 out of 11 who had from 6 red blood cells to loaded as compared with 7 out of 9 for the distance swimmers. Swimming is considered a noncontact sport, so the higher percentage and amount of red blood cells in the distance swimmers is of real significance. It must be the result of the renal response to the exercise alone, and not from any contact renal trauma.

Track.—Track is considered a partially noncontact sport because without doubt the kidneys receive some trauma from the continual jogging up and down during a long-distance race. Figure 3 is divided into short-distance and long-distance events. Individual columns show the 100, 220, 440, and 880 yard and the 1-mile and 2-mile races. One can study this chart in the vertical manner and so compare the differences of the amount of albumin, red blood cells, and casts in short and distance events. By horizontal study one can see either the albumin, the red blood cells, or the casts separately in the various distances, from the 100-yard sprint to the 2-mile race. Scanning the chart in the vertical manner, it is apparent that in the 100-yard dash there are practically no abnormal findings. True there were three who showed some red blood cells and three showed some casts, but they were from 0 to 2 per high-power field. The albumin was only a trace. As one progresses with the distance of the races, from the 220-yard to the 2-mile, in the vertical manner one sees an increase in each after the 220-yard. Beginning with the 440-yard race, all three findings are markedly increased. In the mile race, it is evident that both the number of athletes involved and the degree of abnormalities are precipitously higher. For instance five out of six of the milers had a 3+ albumin. Three out of the six had 3 to 5 red blood cells, and one had 11 to 20 per high-power field. The casts similarly increased: four out of six had from 3 to 10 per high-power field. In the 2-mile race one had a 2+ and



(Numbers indicate athletes.)

Fig. 2—Urinary findings in swimmers in intercollegiate contests, short and distance events.

one had a 4+ albumin level. Both of them had red blood cells 6 to 10 per high-power field; one had 6 to 10 casts per high-power field, and the other was loaded with casts.

Scanning this chart horizontally, one can compare the amount of albumin in all of the various races starting from the 100-yard dash and progres- g to the 2-mile. In the 100-yard and 220-yard s, there is very little present. In the 440-yard, ses considerably. This is also apparent with the d blood cells and casts. These findings are also evident in the 1-mile and 2-mile events. It is apparent that the longer and more strenuous the race, the greater the percentage and degree of abnormal urinary findings.

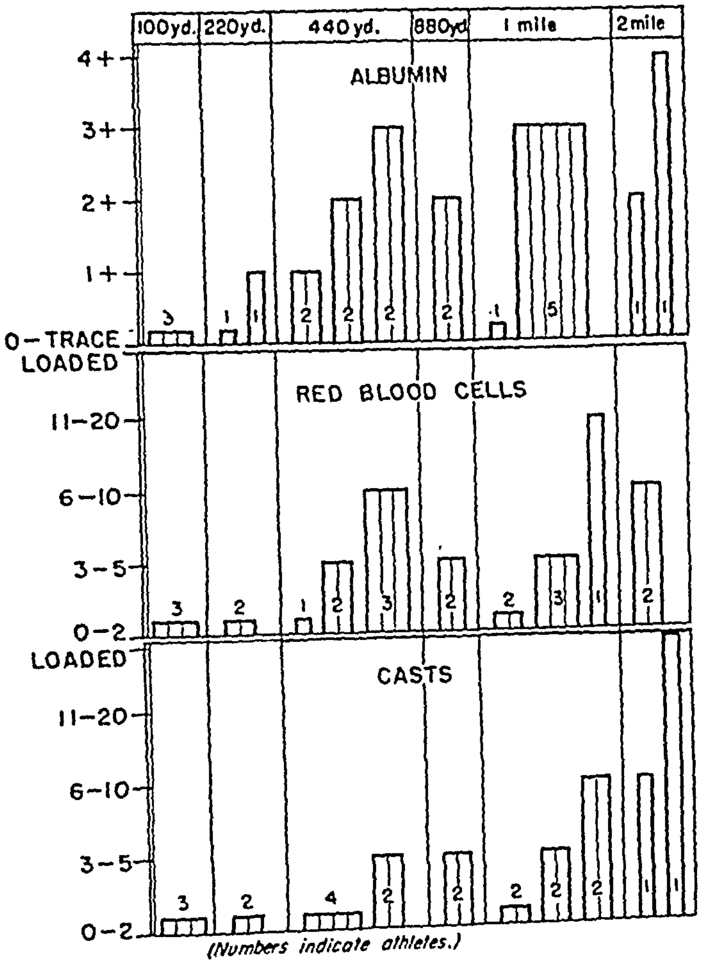


Fig. 3—Urinary findings in track men in intercollegiate contests, short and distance events.

Lacrosse.—Lacrosse is definitely a contact sport. It is a strenuous game with few substitutions or chances for rest. Out of the 16 players there were only 3 who had 0 to trace of albumin, 6 had 1+, 2 had 2+, and 5 had 3+ levels. In the red blood cell counts, four had from 0 to 2, four from 3 to 5, six from 6 to 10, and two over 11 per high-power field. The casts were quite prominent in this sport. Five men had from 3 to 5 per high-power field, one had 11 to 20, and six players were loaded with casts. Here, too, it was noted that the men who played the hardest and the longest were the ones who had the most albumin and casts in the urine. It is also interesting to note that one game was played on a cool, pleasant, breezy day and another on a very hot, humid afternoon. The abnormal urinary findings were definitely higher on the hot day. This was also evident in our studies on the crew men.

Rowing.—Rowing was the first true noncontact sport which one of us (E. P. A.) studied and reported.[6] This study was carried out on four college crews after two practice races and after one intercollegiate race. In the practice session, 31 men were examined before and after exercising, and 16 before and after the intercollegiate race. All the urine specimens before the races were normal in all respects. The relative percentage of the three races are summarized in figure 1. Of the 40 men showing albumin after the intrasquad races, 27 had only a trace and 13 had a 1+ level, 17 or 55% of the men had 1 to 4 red blood cells per high-power field, and casts were found in 16 of these 17 men. After the intercollegiate race, 13 of the 16 men showed albumin, and of these 13, 4 had a trace and 9 had a 1+ to 2+ level. This would seem to show that after an intercollegiate race, which brings forth more effort and severe physical exercise than the intrasquad practice races, the percentages were higher and the degree of abnormalities greater. This difference was also noted in the amount of red blood cells and casts.

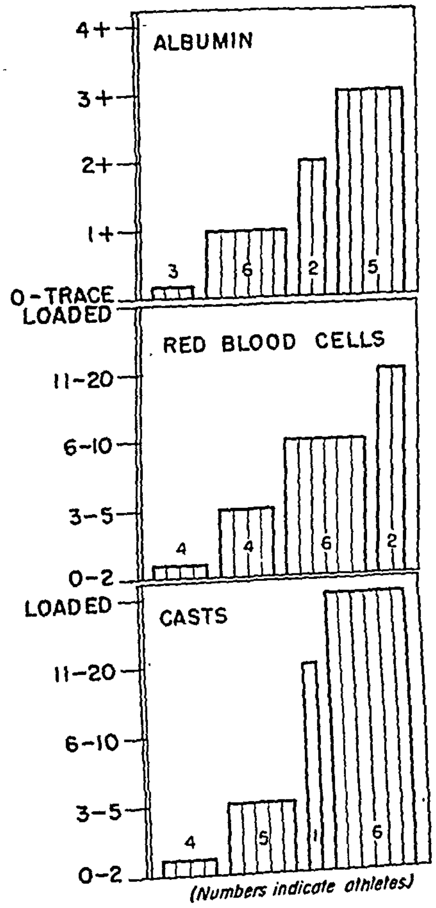


Fig. 4—Urinary findings in lacrosse players in intercollegiate contests.

Comment

The striking thing in these investigations is the apparent uniformity of the findings of albumin, red blood cells, and casts in the urine of most athletes after strenuous exercise. In the traumatic sports such as football, lacrosse, and boxing, trauma may increase the actual number of red blood cells in the urine to a gross hematuria, but the actual percentage of athletes with microscopic hematuria is no higher in those sports than in the nontraumatic sports. Another interesting fact is the uniformity of these abnormal urinary findings contrasted in exercise of short and long durations. This is true in both track and swimming. The difference in findings in the 100-yard and 220-yard dashes as contrasted with the 440-yard, 880-yard, 1-mile, and 2-mile events is evident. The men in the 50-yard and the 100-yard swimming events showed more abnormal findings than the 100-yard track men, evidently because there is much more energy put forth by the swimmers. However, the short-distance swimmers showed less albumin and fewer casts than the long-distance swimmers, such as in the 1,500-meter events. Some of these mile swimmers had a very heavy albuminuria and the microscopic fields were loaded with casts and many red blood cells. The amount of albumin and the casts were the most striking findings. This is also found in the lacrosse players.

It is interesting to speculate from this study whether the slightest injury to the filtration mechanism permits the albumin to leak through and as the injury progresses because of increased exercise the red blood cells and the casts then appear. This seems apparent in the short-distance swimmers. Many of them had few or no red blood cells and casts, but all 11 had albumin, 5 had 1+, and 6 had a 2+ level. This is also suggestive in the track chart. It is believed, and has been proved in track men and in our football and crew studies, that the urine returns to normal within 24 to 48 hours after discontinuing the exercise. However, this particular point was not investigated in this present study.

We thought it would be interesting to determine whether any of this renal response to exercise was related to the nervous state of the individual engaged in these intercollegiate contests. Therefore, we took as test subjects four female college freshmen who were taking their first examination in college. After talking with them, we were convinced that they were just about as highly nervous and tense as anyone could be. Specimens were obtained immediately after their examinations and examined in the usual manner. None of these girls' specimens showed any albumin, casts, or red blood cells. We feel, therefore, that the response obtained in our subjects during exercise is not effected by the slight outpouring of epinephrine which might occur during the period of nervous tension and excitability, but rather is dependent upon the physical exercise itself.

The cause for the presence of albumin, red blood cells, and casts in the urine after severe exercise is not definitely known. There have been interesting hypotheses substantiated by considerable experimental research. It is known that during exercise the blood leaves the splanchnic area and various organs including the kidneys. It is shunted into the main circulation, to the heart, to the lungs and to the muscles involved in the exercise which demand it for their increased metabolism. It is well known that there is a marked decline in the renal plasma flow and the glomerular filtration rate. In severe exercise the plasma flow may be reduced as much as 50 to 75%. Boyarsky[7] reported that in studies on traumatic shock carried on during World War II, half of the patients with a mean blood pressure of 50 mm. Hg showed a reduction in renal blood flow of 30% to 80%, and the remainder showed a more profound reduction. Furthermore, hypoxic damage to the nephron may result from the marked lowering of the renal blood flow. In the dog a 90% reduction in renal blood flow is a critical level below which acute renal failure can be expected to appear, if the reduction persists. Therefore, it is evident that the degree of vascular diversion from the kidney during severe exercise approaches that seen in traumatic shock.

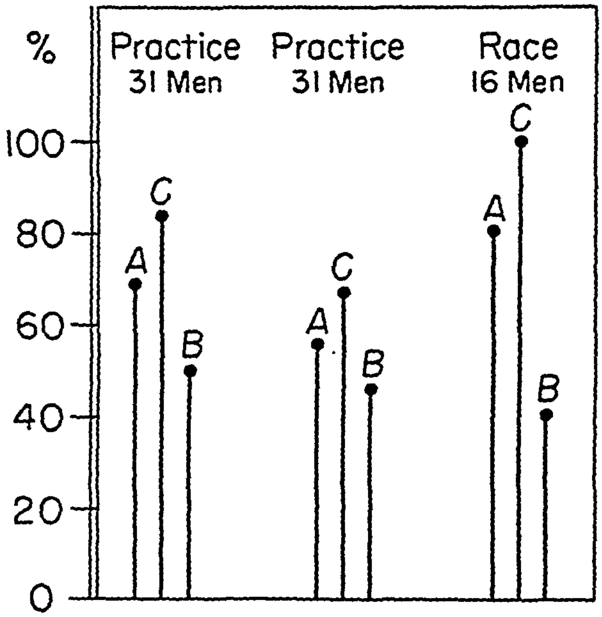


Fig. 5.—Urinary findings in crew men after two practice exercises and an intercollegiate race. A=albumin; B=red blood cells; C=casts. Reproduced with permission of *Southern Medical Journal* (**50**:905-909 [July] 1957).

Chapman and co-workers[8] showed that this reduction does not remain for long. Within an hour after the exercise is stopped, there is a return of the plasma flow to within 10% of the preexercise level. Barclay and associates[9] report a drop in the glomerular filtration rate of 44.6% after exercise. They postulate that the primary change is the constriction of the afferent arterioles. After this there is a compensatory constriction of the efferent arterioles in order to maintain a filtration rate in the face of a falling renal blood flow. In this way the glomerulotubular balance is not upset. The renal vascular channels definitely constrict, and this causes the considerable decrease in the renal blood flow. It may drop from a normal of 1,000 cc. per minute at rest to 200 cc. per minute during exercise. Hence 800 cc. or more of blood per minute is shunted to the active organs where it is most needed.

The constriction during light and moderate exercise is probably a response to specific nerve impulses only. The marked constriction caused by the addition of epinephrine occurs only when the exercise becomes severe. Intravenous administration of arterenol and epinephrine were given to several subjects and measurements made of the renal plasma flow, glomerular filtration rate, urine volume rate, and protein excretion. In their study, King and Baldwin[10] showed the following findings: 1. Transient proteinuria of short duration occurred in all subjects from both arterenol and epinephrine. 2. The injection of epinephrine and arterenol also produced a reduction in renal plasma flow, glomerular filtration rate, and urine volume, with an increase in filtration fraction. 3. The over-all increase in renal vascular resistance occurred in all of these patients, predominately afferent in the case of arterenol and equally afferent and venular with epinephrine. 4. The maximum tubular reabsorptive capacity for glucose is unaffected by arterenol. This is taken to indicate that the renal ischemia is diffuse and involves all of the nephrons and is not selective in character. It would be interesting to determine the pyrocatechin level in the urine of the athletes to see if arterenol plays some part in the vasoconstriction during exercise.

White and Rolf[11] found similar results in PAH and inulin clearance tests after exercise. They both fell markedly, and the renal vascular resistance increased at least fivefold. In these experiments values returned to normal within one hour after the cessation of the exercise. The albumin did not appear in the urine until after the exercise was completed. This suggested the theory of a differential constriction of the renal vascular channels. During exercise, some of the glomeruli may have o blood flow or a capillary pressure too low to permit filtration. Then when the flow and filtration are reestablished after the exercise is over, the albumin appears in the filtrate of these so-called damaged glomeruli. If the blood flow is uniformly reduced by vasoconstriction through the glomerulus, one would expect the albumin to appear during the period of greatest ischemia. This could be proved if it could be shown that the glucose tubular maximum capacity is reduced during exercise. For in health, the constancy of glucose tubular maximum for the reabsorption of glucose suggests that all the nephrons are functioning. If this drops, some of the glomeruli must be nonfunctioning. This would be in favor of the selective constriction theory. King and Baldwin[10] showed that in their subjects the maximum tubular reabsorptive capacity for glucose is unaffected by arterenol, indicating that the renal ischemia diffusely involves all of the nephrons.

Proteinuria is evidence of damage to the glomerular filtration mechanism which has not been compensated by the tubular reabsorption as is normally carried out. The nature of the protein excreted during exercise may shed light on the size of the glomerular pore allowing its passage, whether it is a normal membrane or an anoxic rupture. This can be determined by the method of paper electrophoresis. Boyarsky[7] hypothesized that during severe renal ischemia, the tubules become unsaturated in respect to the load received from the glomerulus, since the filtration rate has fallen to low levels. The tubular reabsorption becomes excessive. The urine flow diminishes greatly and the urine becomes overly concentrated. In patients in shock, even though the renal blood flow drops to 5%, urine formation still continues. This does not cease until the renal blood flow stops. Therefore, he concludes that the cylindruria is evidence of inspissation of protein in the tubule due to the diminished urinary volume or complete stagnation. The morphologic picture of the kidney after ischemic injury is a focal necrotic lesion located at any portion of any tubule as if by chance. It has been called "tubulorrhexis." It shows the disruption of the basement membrane and the tubular cells so that there is a gaping hole which could serve for back flow of urine or as a tubular venous anastomosis.

It is doubtful that this is what takes place after exercise because of the rapid recovery of the tubular cells. Usually within 24 hours the albumin, casts, and red blood cells have disappeared from the urine. This could be studied by the renal biopsy method in experimental animals. The finding of albumin in the urine in conditions other than definite renal disease is not uncommon. For instance, orthostatic albuminuria in the tall, asthenic young man is probably due to circulatory changes resulting in diminished renal blood flow. Such transitory albuminuria is inconsistent with the idea of tubulorrhexis. Would an actual rupture of membrane or cells heal so promptly? However, the large amounts of red blood cells, albumin, and casts in the urines of the distance swimmers and track men after severe prolonged exercise make us believe that under such circumstances there is definite renal damage. Boyarsky states that whether this is evidence of minute foci of renal destruction, which is not noticed because of the normally large renal reserve, or is a damage on the cellular level, which is readily reversible, we can not say.

In addition to the above-mentioned changes in the urine, after exercise, Hyman and co-workers[12] reported an increased exfoliation of epithelial cells. Many of these cells come from the deeper layers of the bladder epithelium. The cause suggested is that the urine swirling over the bladder mucosa mechanically causes an increase in this exfoliation. Certainly there can be no effect on the tissues themselves. It is a purely local condition in the bladder and not due to lesions elsewhere in the urinary tract.

Conclusions

The above results in the sports of rowing, football, track, lacrosse, and swimming show the constancy of the abnormal elements in the urinary sediment. Disregarding the theoretical cause, the fact remains that, at least temporarily, there is damage to the kidney. Whether this leaves the tubular element in a weakened or more vulnerable condition cannot be proved. We are inclined to believe that it does. The recovery seems to be prompt, but is it complete? The question arises as to whether anyone who has had definite renal disease such as acute glomerulonephritis or pyelonephritis should indulge in severe physical exercise. Exercise at least temporarily adds additional damage to the already injured renal cellular elements. We can recall two such instances of men who continued to indulge in severe physical exercises in intercollegiate athletic contests after having had acute nephritis. One of these men died in renal failure within 5 years and the other within 15 years of the acute renal disease. Both of these men had apparently recovered from their acute nephritis. They returned to college and again took active part in intercollegiate athletics. The question is, was the renal failure hastened by the added strain of exercise? Another patient had an attack of acute pyelonephritis. This apparently cleared up promptly on chemotherapy, as shown by negative cultures and negative microscopic stained smears. Within two weeks she began playing strenuous tennis singles. She had a relapse the day after such a contest. Is it advisable for anyone who has had acute renal injury to ever indulge in severe physical exercises? Is it not adding insult to injury? We believe that we should recommend limitation of exercise in patients with impaired renal function or history of acute or chronic parenchymal renal disease.

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AIR POLLUTION AND PULMONARY CANCER.—Carcinogenic agents belonging to the group of polycyclic aromatic hydrocarbons, to the aliphatic epoxides, and to inorganic compounds containing chromium and nickel have been identified in the atmosphere. One of the most ubiquitous of the carcinogenic agents belonging to the polycyclic aromatic hydrocarbon group of chemicals is 3,4-benzpyrene. It is derived as an atmospheric pollutant from many sources including gasoline and diesel engine exhausts, soot secondary to the incomplete combustion of organic matter, soot incidental to rubber-tire wear and tear and degradation, and in isolated areas as specific industrial effluents in the manufacture of coal tar and its derivatives. The aliphatic materials are primarily introduced into the atmosphere as a result of pollution by raw gasoline vapors. These vapors, under certain meteorologic conditions, react in the presence of sunlight and oxides of nitrogen to form a broad spectrum of hydrocarbon oxidation products. Chromium and nickel though present in infinitesimal amounts nevertheless must be considered by virtue of occupational and experimental data incriminating them as carcinogenic agents. It must be remembered that one of the critical factors in eliciting the carcinogenic responses is the concentration at which these agents are present.—H. L. Falk, Ph.D., Pulmonary Cancer with Special Reference to Air Pollution and Pathogenesis, *CA Bulletin of Cancer Progress*, March-April, 1958.

J.A.M.A., June 14, 1958

DIURETIC ACTION OF TWO CARBONIC ANHYDRASE INHIBITORS IN CONGESTIVE FAILURE

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Two carbonic anhydrase inhibitors, acetazolamide and ethoxzolamide, were compared with intramuscularly given meralluride by oral administration in a group of ambulatory patients with congestive heart failure, with the criterion of response being the loss of body weight during the first 24 hours after the dose. The maximum diuretic response to acetazolamide was equal approximately to that given by 0.5 cc. of meralluride; the response to ethoxzolamide was somewhat greater, equal approximately to that given by 0.7 cc. of meralluride. The diuretic responses to the two carbonic anhydrase inhibitors were similar when they were given in doses which caused approximately the same incidence of unpleasant symptoms. The maximum diuretic effect of acetazolamide was obtained from a dose of 125 mg. No greater effect was obtained from a dose eight times larger. It was found that orally given acetazolamide neither increases nor diminishes the diuretic response to intramuscularly given meralluride.

Since the report by Friedberg, Taymor, Minor, and Halpern[1] on the use of acetazolamide (Diamox), a specific carbonic anhydrase inhibitor, as an orally given diuretic in patients with congestive heart failure, the investigation of this class of compound has rapidly advanced and many publications have appeared describing their pharmacology and clinical applications. Several new members of the carbonic anhydrase inhibitor group have been tested, although most of the reports relate to acetazolamide. While agreement is general that this compound produces diuretic effects which prove useful in milder cases of congestive failure although insufficient in more advanced cases, there remain unsettled problems which are in need of more study before the final place of these materials in diuretic therapy is established. More needs to be known about their potency in relation to a standard and to other orally given diuretic agents, the most favorable dosage and dosage plans, and their effect when used together with other diuretic agents. In previous reports,[2] we described a method of bioassay of diuretic agents in ambulatory patients with congestive failure. We have now applied this method in an examination of acetazolamide and of a new chemically allied carbonic anhydrase inhibitor, ethoxzolamide (Cardrase). The results form the subject of this report.

Method of Bioassay

We adapted the conventional principles of pharmacological assay on animals to the assay of diuretic agents in patients with congestive failure. he test drug is compared with a standard—intracularly given meralluride (Mercuhydrin) sodium—in a group of 25 or more ambulatory patients with congestive failure in attendance at our cardiac clinic. The criterion of response is the body-weight loss in the first 24 hours after the dose. This closely parallels the curve of clinical improvement in patients with congestive failure.[3] The patients are accurately weighed, receive a dose of the drug, either meralluride given intramuscularly or the particular test-drug, and are weighed again 24 hours later. They return for a dose of the drug at weekly intervals. These patients are instructed to remain on their usual diet, with free water intake and salt restriction. Most of them also receive a daily dose of a digitalis glycoside. This regimen remains unchanged during the assay. In each group of patients, several dose-levels of the standard and of the test-drug are administered in randomized fashion. The average weight loss for the group with the various doses provides data for dosage-response curves for both the standard and the test-drug in the same patients. The potency of the test-drug is expressed in terms of the standard. Differences in response are tested for significance by standard statistical methods. In the case of the assay of orally given diuretics which may produce disagreeable symptoms from their local actions, an inert placebo tablet indistinguishable from the test-drug is included in the assay by the double-blind technique.[4]

Acetazolamide—Potency and Dose

In the clinical evaluation of this material, Friedberg and others[1] used single doses as high as 0.75 Gm. three times daily for two or three days and as low as 0.25 Gm. daily continuously for longer periods. They found the 0.25-Gm. dose as effective as the higher ones. They observed in their group of 26 patients that about 70% showed a diuresis, weight loss, and clinical improvement, which compared favorably with the results of a mercurial diuretic given parenterally. Belsky[5] found acetazolamide a satisfactory substitute for

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the 2-cc. injection of meralluride in 11 of 13 patients with congestive failure treated for prolonged periods. He used a daily dose of 1 Gm., which caused some toxic effects, but in two cases he also observed that the 0.25-Gm. daily dose was equally effective and suggested that this dose might prove the most favorable for both starting and maintaining the treatment. The fact that in these studies there were patients in whom acetazolamide proved unsatisfactory so that the return to the mercurial injection was necessary points to the limited diuretic action of acetazolamide as compared with the organic mercurial. Clinical experiences such as these are useful but do not provide a quantitative value for the relative diuretic activity of different materials. Moyer, Ford, and Spurr[6] compared orally given acetazolamide with meralluride injection in terms of the 24-hour increase in sodium excretion in patients on a fixed salt and water intake. Their chart shows that the 0.25-Gm. dose of acetazolamide produced only about one-fourth the effect of an injection of 2 cc. of meralluride. They observed that larger doses produced no greater effect. They further observed[7] that the 0.25-Gm. orally given dose of acetazolamide produced the same effect as a dose of 3 tablets (30 mg. of nonionic mercury) of an orally administered mercurial diuretic, chlormerodrin (Neohydrin). This also indicates a restricted order of potency of acetazolamide since, in our bioassay,[2b] more than twice as much chlormerodrin given orally produced diuretic effects equal to 0.71 cc. of intramuscularly given meralluride. In contrast with these findings is the report by Cardillo, Mullin, Schiffer, and Lyons.[8] They carried out a bioassay in accordance with conventional principles and compared orally given acetazolamide with an injection of mercaptomerin (Thiomerin) sodium in terms of the 48-hour weight loss in 25 ambulatory patients with congestive failure. With respect to acetazolamide their results show that the 0.5-Gm. dose caused nearly twice the effect of the 0.25-Gm. dose (ceiling effect at about 0.5 Gm.). Their results further indicate that acetazolamide is more effective than the injection of mercaptomerin, the 0.5-Gm. dose causing more than twice the effect of the 1-cc. injection of mercaptomerin, the maximum effect greater than the 2 cc. of mercaptomerin (approximately the ceiling dose of the organic mercurial injection[9]). This result with mercaptomerin could be an artifact due to the method, the use of the weight loss over a 48-hour period, the acetazolamide having been given for two days and the mercaptomerin for only one day per week. Since a large part of the weight loss from a dose of mercaptomerin is recovered on the second day, their results may have involved a comparison of the maximum effect of acetazolamide with only a partial effect of the organic mercurial.

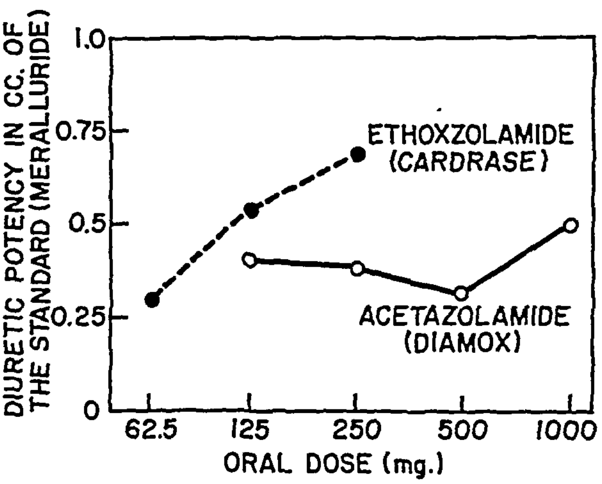

Fig. 1.—Diuretic potency of two carbonic anhydrase inhibitors in terms of intramuscularly given meralluride in patients with congestive failure; 24-hour weight loss is index of effect. Position of points on curves was obtained by comparing average weight loss for group at each dose level with dosage-response curve of intramuscularly given meralluride administered concurrently to same patients.

Incidence of Toxic Symptoms After Oral Administration of Two Carbonic Anhydrase Inhibitors

	Dose, mg.	Doses Given, No.	Patients Reporting Symptoms, %		
			None	Minor	Major
Acetazolamide	125	154	88	11	1
	250	188	85	12	3
	500	38	71	10	19
	1,000	37	65	14	21
Ethoxzolamide	62.5	42	98	2	0
	125	89	71	19	10
	250	47	51	26	23

Dosage-response curves are an essential part of a satisfactory bioassay. Ford, Spurr, and Moyer[7] stated that the range of doses of the anhydrase inhibitors for the minimal (threshold dose) and maximal ("apex point" or ceiling dose) action of increasing salt and water is so small that it is impossible to establish a satisfactory dosage-response curve. Cardillo and others[8] obtained a favorable dosage-response curve with acetazolamide, with use of the criterion of the 48-hour weight loss. We failed to obtain a dosage-response curve with the 24-hour body weight loss as an index and did not pursue the experiment to a definitive bioassay, although it is probable that a dosage-response curve would have been obtained if smaller doses had been tried. As far as we have gone, however, the results give a fairly good indication of the diuretic potency of acetazolamide in terms of the effect of injected meralluride. Our ambulant group of patients with congestive failure received a total of 417 doses of acetazolamide, ranging from 125 to 1,000 mg. each (see the table and fig. 1). The diuretic response was indistinguishable over the eightfold range of doses, all producing a diuresis equivalent to less than that with 0.5 cc. of intramuscularly given meralluride. The dose of acetazolamide for the maximum average diuretic response (ceiling dose) is here on the order of 125 mg. or less. This corresponds to the findings of

Ford, Spurr, and Moyer[7] and is at variance with the observations of Cardillo, Mullin, Schiffer, and Lyons.[8]

Combined Action of Meralluride and Acetazolamide

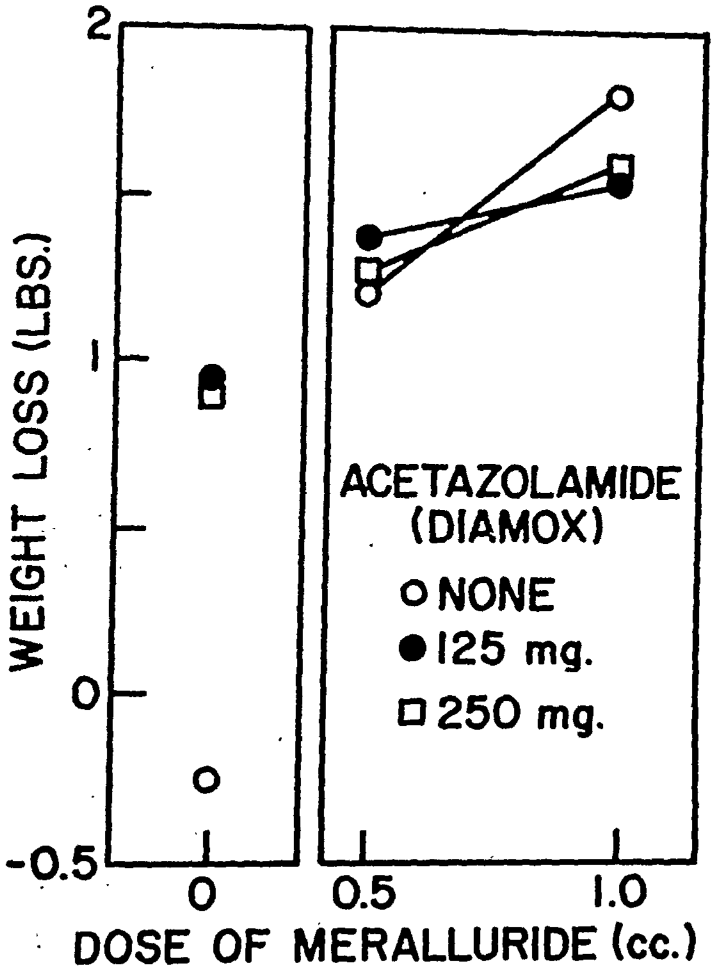

Fig. 2.—Effect of combined administration of meralluride intramuscularly and acetazolamide orally in 39 patients with congestive failure. Acetazolamide does not enhance diuretic response to meralluride.

There are many reports in the literature on the combined administration of various diuretic agents in the endeavor to increase the therapeutic effect. In previous studies we applied our bioassay method in a comparison of meralluride alone with meralluride and ammonium chloride[10] and meralluride and aminophylline.[11] Both of these drugs, as others have observed,[12] were found to enhance the diuretic effect of the particular injection of meralluride. We have now tested acetazolamide in the same way. The results are shown in figure 2. The acetazolamide was given in doses producing average maximum diuretic effects, 125 and 250 mg. each. The effect of the acetazolamide alone was compared with that of an inert placebo tablet. The points relating to this in figure 2 are based on nine randomized doses in each of 39 patients. The acetazolamide gave an average weight loss of nearly 1 lb. (0.5 kg.) in 24 hours, which proved to be an unequivocal diuretic effect. The difference between the acetazolamide and the placebo was highly significant ($p<0.01$) by paired t-value analysis. When the tablet of acetazolamide was given together with an injection of meralluride, the diuretic effect proved to be that of the meralluride alone. The three curves in figure 2, one for the meralluride alone and two for the combination with acetazolamide, are substantially similar. This was confirmed by statistical analysis. There were three separate meralluride dosage-response curves, and calculation revealed no significant effect of the acetazolamide on either slope or displacement. By analysis of variance restricted to the four doses that included both drugs, it was possible to show a significant effect for the meralluride but not for the acetazolamide and neither enhancement nor depression of the meralluride effect by acetazolamide. Maren[13] tested the combined action of the two drugs in dogs in terms of sodium excretion and concluded that their primary renal effects are not additive but that metabolic acidosis due to acetazolamide increases the response to meralluride. In a study of patients with congestive failure refractory to meralluride, Rubin, Thompson, Braveman, and Luckey[14] found acetazolamide alone ineffective. The mild metabolic acidosis produced by acetazolamide also failed to restore the diuretic response to meralluride significantly until more pronounced acidosis was produced with the aid of large doses of ammonium chloride.

Ethoxzolamide

Ethoxzolamide, 6-ethoxy-2-benzothiazolesulfonamide (Cardrase), is a new carbonic anhydrase inhibitor which is under consideration for therapeutic use. Chemically, it is closely allied to acetazolamide. Ford, Spurr, and Moyer[7] compared it with acetazolamide in patients with congestive failure, using as an index the 24-hour urinary sodium excretion. With this compound they obtained a conventional dosage-response curve, with increasing effects with doses of 33.75 to 125 mg. and with larger doses up to 500 mg. producing no greater effects than the dose of 125 mg., and they stated that this was substantially similar for acetazolamide. They concluded that the diuretic activity of ethoxzolamide is not significantly different from that of acetazolamide in terms of electrolyte and water excretion and change in body weight.

Our assay was carried out on 42 ambulant patients with congestive failure, the comparison being made with intramuscularly given meralluride in the same patients in terms of 24-hour body-weight loss. There were 178 doses of 62.5 to 250 mg. each. Higher doses could not be tested because of the mounting incidence of disagreeable symptoms. The results are charted in figure 1. A conventional dosage-response curve was obtained. In this assay, ethoxzolamide proved to be substantially more potent than acetazolamide when compared with intramuscularly given meralluride not only from the standpoint of the dose necessary for a particular effect but from the standpoint of the maximal obtainable effect (ceiling response). The 250-mg. dose produced a diuretic response equivalent to that with approximately 0.7 cc. of intramuscularly given meralluride. There are no facts available at present to explain the higher ceiling response to ethoxzolamide than to acetazolamide, since both are carbonic anhydrase inhibitors. There remains the possibility that an action in addition to anhydrase inhibition may be involved.

Toxicity

The reports in the literature indicate a low order of toxicity for the carbonic anhydrase inhibitors as orally administered diuretics. This is confirmed in the present study. On each clinic visit, every patient received both an intramuscular injection and an oral capsule, at least one being an inert material. All judgments were made against that placebo background 24 hours after the dose by an examiner who did not know the identity of any particular dose (double-blind test). Persistent placebo reactors thus could be discounted, although an occasional report may still include a symptom not caused by the pharmacological action of the drug. Symptoms were classified as "minor" when they did not jeopardize the regimen of treatment (weakness, chills, grogginess, dizziness, dry mouth, flushed face, itching face, tingling fingers, headache, and slight nausea). They were classified as "major" when they were judged severe or disturbing enough to cause some patients to refuse further medication or to continue only under protest (severe nausea, diarrhea, abdominal cramps, and vomiting). The results are presented in the table. The incidence of disagreeable symptoms increased with the dose. It rose with the larger doses of both drugs to approximately one-fifth of the group of patients. A more extensive experience is necessary to establish the relative incidence of toxic effects of the two agents in relation to the doses that produce the maximum diuretic effects.

Summary and Conclusions

The diuretic potency of two carbonic anhydrase inhibitors, acetazolamide (Diamox) and a new compound, ethoxzolamide (Cardrase), in ambulant cardiac patients with congestive failure was determined by comparison with a standard, intramuscularly given meralluride (Mercuhydrin).

The method of bioassay involves a dosage-response curve for the test-drug and the standard in the same group of 25 or more patients in terms of the 24-hour weight loss. This index of effect corresponds to clinical improvement. The validity of differences in response is tested by conventional statistical methods.

The average maximum diuretic response with orally given acetazolamide is obtained from a dose of approximately 125 mg. The average maximum diuretic effect of this drug (ceiling effect) is equivalent to somewhat less than that with 0.5 cc. of intramuscularly administered meralluride. An average maximally effective oral dose of acetazolamide given together with an intramuscular injection of meralluride does not enhance the diuretic response to the latter. Ethoxzolamide is a somewhat more potent diuretic agent than acetazolamide both on a weight basis of the compounds and from the standpoint of the maximum obtainable diuretic response. It is suggested that an action in addition to anhydrase inhibition may explain the difference. The average maximally effective dose of ethoxzolamide produces a diuretic effect about equivalent to that with approximately 0.7 cc. of intramuscularly given meralluride.

1300 York Ave. (21) (Dr. Gold).

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The ethoxzolamide used in this study was supplied as Cardrase by the Upjohn Company, Kalamazoo, Mich.

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RESULTS OF LONG-TERM USE OF TOLBUTAMIDE (ORINASE) IN DIABETES MELLITUS

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Factors favoring success with tolbutamide in the treatment of diabetes were sought in a study of 1,030 diabetic persons. There were 772 in whom it was deemed feasible to begin maintenance studies with tolbutamide alone. In 136 of these, trial indicated within a month that tolbutamide alone was inadequate (primary failure). In 407 patients in whom good control of hyperglycemia and glycosuria was obtained, important characteristics were that the onset of diabetes had usually occurred after the age of 40 years and that the insulin requirement was less than 20 units daily. In 40 patients results with tolbutamide became unsatisfactory after an earlier period of good control (secondary failure). A single-dose, four-hour response test was helpful in selection of patients for long-term maintenance therapy with the drug. There were only eight patients in whom the use of tolbutamide had to be stopped because of side-effects; the symptoms of toxicity were generally urticaria and minor digestive complaints. Histological examination of liver and pancreas was carried out in 2 of 12 patients who died of various causes during the period of observation; no evidence of damage attributable to the drug was obtained. Since tolbutamide is taken orally, it is especially welcome to patients handicapped by blindness or by other conditions which make self-injection difficult. It should not be used if dietary restriction alone will suffice or if tolbutamide is not effective and insulin is found necessary to provide good control.

Experience with sulfonylurea compounds in patients with diabetes began in the Joslin Clinic in December, 1955, with the use of carbutamide (BZ 55). Tolbutamide (Orinase) was used first in February, 1956. Experience here as elsewhere throughout the world has amply confirmed the blood sugar lowering effect of these agents, as found earlier in clinical trials in Germany.

Although Janbon [1] and Loubatières [2] and their co-workers as early as 1942 had described the hypoglycemic effect of certain sulfonamides and in the ensuing years continued to carry out studies with these compounds, Franke and Fuchs [3] were the first to use a related chemical agent, BZ 55, in the treatment of diabetes. Carbutamide (1-butyl-3-sulfonylurea) was subjected to fairly extensive clinical trial in the United States and Canada from late in 1955 until the fall of 1956, when it was withdrawn from use with patients because of a high incidence of toxic manifestations including allergic skin rashes, jaundice, leukopenia, thrombocytopenia, and agranulocytosis.[4] In addition to these untoward effects, carbutamide has the disadvantage that it is bacteriostatic, with some influence on the intestinal flora and the development of sulfonamide-resistant strains of bacteria in the body.[5]

Tolbutamide (1-butyl-3-*p*-tolylsulfonylurea), known first in Germany as D 860, Rastinon (Hoechst), or Artosin (Boehringer) [6] and in the United States as Orinase,[7] differs chemically from carbutamide only in having a methyl group substituted for the amino group in the para position on the benzene ring. This slight difference brings about three changes in properties: 1. Tolbutamide is not

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bacteriostatic. 2. In the same dosage, tolbutamide is not quite as hypoglycemic as carbutamide, probably due to its more rapid excretion.[8] 3. Tolbutamide so far has shown itself to be much less toxic than carbutamide.

In the present paper are summarized our results with the long-term use of tolbutamide. In addition, there will be outlined some guiding principles for the use of this drug.

Material and Methods

From February, 1956, until Nov. 10, 1957, we gave tolbutamide at one time or another to 1,030 patients with diabetes. The group comprised ambulatory patients seen at the Joslin Clinic, inpatients at the New England Deaconess Hospital, and summer campers at the Elliott P. Joslin and Clara Barton Birthplace Camps for diabetic children. Except for children and other selected persons given single-dose response tests and except for certain subjects chosen at random, particularly in the early months of the study, patients with whom the tolbutamide trials were carried out were in general those above the age of 40 years and those whose insulin requirement was below 40 units a day. The group studied was, therefore, a selected one, although no strict rules were followed in this regard.

Early in the study a sulfonylurea response test was devised in order to have some way of determining in advance those patients most likely to respond favorably to the drug in maintenance studies. The procedure used was as follows: 1. In adult patients with stable diabetes under control with small doses of insulin, omit insulin during the two days immediately preceding the test day. If the dose is 20 units or more daily or if omission of insulin seems potentially dangerous, give crystalline insulin in appropriate dosage during these two days. 2. On the day of the test, withhold insulin and food until the test has been completed. 3. Determine the blood sugar level with the patient in the fasting state. 4. Give (to adults) 3 Gm. of tolbutamide by mouth. 5. Determine the blood sugar level four hours after administration of the drug.

In the original interpretation [9] of findings during the response test, a satisfactory result was considered to have been secured if within four hours there was a fall in blood sugar level of more than 20% of the initial value. In a recent analysis of results, this was found not valid at all levels of initial blood sugar and so a change in criteria was made which will be discussed in the section entitled Sulfonylurea Response Test.

Various methods of establishing the dosage of tolbutamide were used. At first many patients were given 3 Gm. daily for one or two days, then 2 Gm. daily for one or two days, and finally a maintenance dose of usually 1 Gm. a day. More recently, patients found to be quite responsive to the drug in the test just described have been started at once on therapy of 1 Gm. daily, with success. In general, the entire dose has been given daily before breakfast. However, in some instances, particularly in those patients whose maintenance requirement proved to be more than 1 Gm. daily, the dose was divided by giving some of the drug before breakfast and some before supper, with the larger part before breakfast. This division of dosage is justified by a consideration of the length of time a given dose of tolbutamide provides an effective blood level of the drug, namely 8 to 10 hours. Relatively few patients complained of local gastric irritation after taking the drug; in these the tablets may be given satisfactorily with meals rather than on an empty stomach.

Early in the study it was found desirable to set up standards of control in order to have a uniform method of evaluating results. Consequently, satisfactory levels of blood sugar and amounts of sugar in the urine were arbitrarily chosen. These are given in table 1.

TABLE 1.—*Blood Sugar Levels and Amounts of Sugar in Urine Used as Standards of Control**

	Degree of Control†			
	Good		Fair	
Relation to Food	Blood Sugar, Mg./100 Cc.‡	Urine Sugar, %	Blood Sugar, Mg./100 Cc.‡	Urine Sugar, %
Fasting	110	Trace	130	0.1
1 hr. p.c........	150	0.3	180	0.5
2 hr. p.c........	130	0.1	150	0.3
2 hr. p.c........	110	Trace	130	0.1
Urine sugar in 24 hr.	2 Gm. or less		5 Gm. or less	

* For the purpose of classification as to degree of control, the majority of values must conform with the standards listed in the table. All others are considered poor.

† These standard values are the highest acceptable.

‡ "True" glucose as determined by the Somogyi-Nelson procedure.

In order for results to be regarded as "good" or "fair," respectively, it was required that the majority of the blood sugar values fall within the limits prescribed in table 1. An exception was made in those instances in which the trend in most recent tests was definitely toward poorer or better results, as the case might be. Blood sugar determinations were made on both capillary and venous blood with use of the Nelson modification [10] of the Somogyi procedure, which yields values for true glucose. These values average 20 to 25 mg. per 100 cc. lower than those obtained by Folin-Wu or comparable procedures. Sugar in urine was determined quantitatively by the Sumner-Exton method using di-nitro salicylic acid.[11]

Early in the studies, serial white blood cell counts were carried out but were later discontinued since no instance of leukopenia or agranulocytosis was encountered. Extensive studies of liver function were done throughout the period of tolbutamide administration; the results will be published in a separate paper.[12]

Careful adherence to diet was urged with all patients. The composition of the diets was the same as that with comparable patients treated with insulin and provided usually 150-200 Gm. of carbohydrate, 60-100 Gm. of protein, 60-100 Gm. of fat, and 1,400-2,100 calories daily. The body weight obtained at each examination of the patient often furnished a clue as to the probable degree of cooperation of the patient as regards diet.

Presentation of Data

In figure 1 is shown graphically the outcome of treatment of patients given tolbutamide. Of 1,030 patients who at one time or another were given the drug, 227 had the single-dose response test only; most of these were children in summer camps and the subjects of a special study, the results of which have been reported.[13] In addition, for 21 patients data were insufficient and 10 others were treated with both tolbutamide and insulin. Based on experience with the last-named group and with a larger number of patients treated for short periods of time with both tolbutamide and insulin, our impression is that little or nothing is to be gained by such combined treatment.

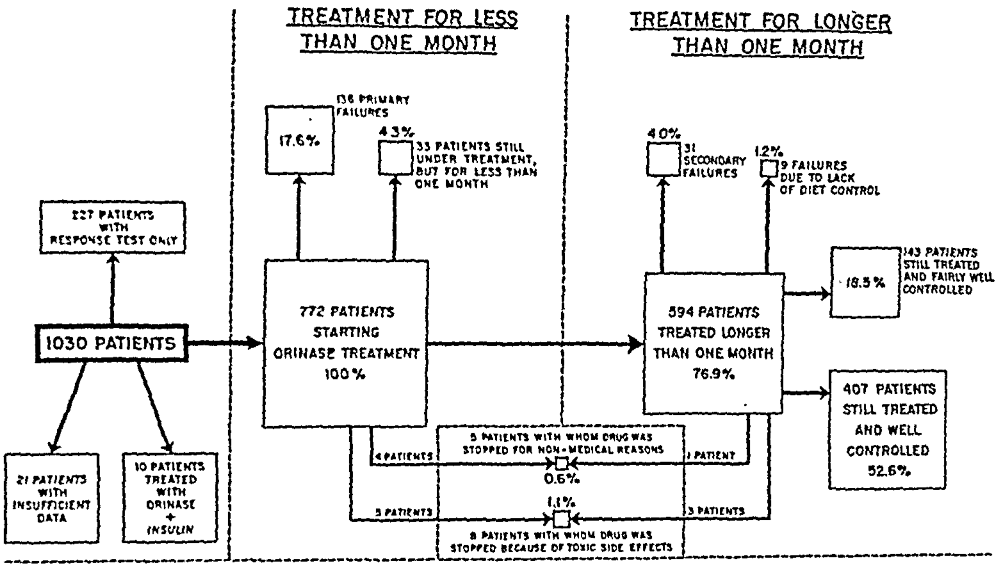
TREATMENT FOR LESS THAN ONE MONTH
TREATMENT FOR LONGER THAN ONE MONTH
1030 PATIENTS
227 PATIENTS WITH RESPONSE TEST ONLY
21 PATIENTS WITH INSUFFICIENT DATA
10 PATIENTS TREATED WITH ORINASE + INSULIN
772 PATIENTS STARTING ORINASE TREATMENT 100%
17.6%
136 PRIMARY FAILURES
4.3%
33 PATIENTS STILL UNDER TREATMENT, BUT FOR LESS THAN ONE MONTH
594 PATIENTS TREATED LONGER THAN ONE MONTH 76.9%
4.0%
31 SECONDARY FAILURES
1.2%
9 FAILURES DUE TO LACK OF DIET CONTROL
18.5%
143 PATIENTS STILL TREATED AND FAIRLY WELL CONTROLLED
407 PATIENTS STILL TREATED AND WELL CONTROLLED 52.6%
5 PATIENTS WITH WHOM DRUG WAS STOPPED FOR NON-MEDICAL REASONS
4 PATIENTS
1 PATIENT
0.6%
1.1%
5 PATIENTS
3 PATIENTS
8 PATIENTS WITH WHOM DRUG WAS STOPPED BECAUSE OF TOXIC SIDE EFFECTS

Fig. 1.—Outcome of treatment in 772 selected patients given tolbutamide.

After elimination of the above-mentioned groups, 772 patients were left on whom maintenance studies were actually begun with tolbutamide alone. With 136 (17.6%) of these, the result was a "primary failure," i. e., within one month it became apparent that blood and urine sugar values were sufficiently abnormal to demand the classification of a "poor" result (table 1). It must be admitted that in a certain few of these patients the treatment has been continued for periods beyond one month at the patient's insistence, or with the hope of eventual success, or because of compelling reasons such as blindness of the patient.

As indicated in figure 1, there were an additional 33 patients, or 4.3% of the total of 772, whose response to treatment has been satisfactory but who have been excluded from further consideration because the total length of treatment at the time of conclusion of the study was less than one month.

Among the total of 772 patients were 8 in whom the drug was discontinued because of side-effects consisting of transient allergic dermatitis, jaundice (one case in a patient with cirrhosis of the liver), and mild digestive disturbances. In an additional five patients the treatment was discontinued for nonmedical reasons. The side-effects will be discussed in more detail later in the paper.

With the above exclusions, 594 patients, or 76.9% of the total, were left for consideration. These patients received tolbutamide for periods ranging from 1 to 20 months (table 2). Of these, good control of blood and urine sugar levels was obtained in 407 patients (52.6% of the total of 772 patients) and fair control in 143 patients (18.5% of the 772 subjects). Thus, of the total of 772 patients, 71.1% responded satisfactorily during long periods of maintenance therapy with tolbutamide. With a few exceptions, such as those who have died intercurrently and those who are now treated with a restricted diet alone, these patients are still receiving the drug.

As is evident from figure 1, 31 patients who originally responded satisfactorily to tolbutamide later did not do so. The cause of these "secondary failures" is not clear and will be discussed later. However, in nine additional patients the secondary failure seemed almost surely due to increasing negligence of the patient as regards diet. Such lack of adherence to diet was usually reflected in significant gain in body weight. These two groups combined gave a total of 40, or 5.2%, secondary failures.

Side-effects.—Because of untoward effects encountered with carbutamide (BZ 55), early in the experience with tolbutamide fear was expressed that use of the drug would be limited by toxic side-effects. However, results to date indicate that the incidence of untoward effects is extremely low. The chief problem, therefore, is not toxicity of tolbutamide but rather the harmful effects of uncontrolled diabetes in patients unwisely chosen for tolbutamide treatment.

Figure 1 lists 8 (1.1%) of the 772 patients in whom tolbutamide treatment was discontinued because of toxic side-effects. In four of these, allergic skin rashes developed. In three others, the treatment was stopped because the patients complained variously of itching of the face, heartburn, chills, epigastric pain, nausea, or acid regurgitation. The symptoms were mild and of questionable relation to the drug therapy. In one patient with cirrhosis of the liver, esophageal varices, and hepatosplenomegaly, jaundice occurred three months after beginning tolbutamide therapy. It is difficult in this patient with serious liver disease to decide whether the jaundice was due to the drug; this problem is discussed in greater detail elsewhere.[12]

Fatal Cases.—During the period of observation 12 patients died who had received tolbutamide for varying periods of time. Among these, the cause of death was myocardial infarction in seven cases. One death was reported from each of the following causes: acute congestive heart failure; probable cancer, site not known; possible diabetic coma; cerebral thrombosis; and fracture of thigh. In only two instances was a postmortem examination carried out. A 69-year-old man who had diabetes of almost 16 years' duration died of myocardial infarction after having received tolbutamide for five and one-half months. A 78-year-old man with diabetes of four and one-half months' duration died of acute congestive heart failure after having received tolbutamide for four months. On histological examination, in neither case did the pancreas show any evidence of damage to the alpha or beta cells nor did the liver show any changes which might be attributed to the drug.

TABLE 2.—*Duration of Treatment in 594 Patients on Tolbutamide Therapy for Longer Than One Month**

Result of Treatment	Patients Receiving Tolbutamide for Number of Months Indicated†																				Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
Good control	26	43	54	46	36	37	21	12	21	24	18	18	10	12	10	5	5	5	1	3	407
Fair control	7	14	7	15	15	19	9	7	6	4	8	15	4	2	1	2	6	1	1	...	143
Secondary failures	5	3	7	5	5	...	2	2	2	...	...	...	...	...	...	...	...	...	...	...	31
Diet failures	1	1	...	1	...	...	...	...	3	...	1	1	...	1	...	...	...	...	...	...	9

* Not tabulated are 4 patients with whom, after one month of treatment, tolbutamide was discontinued (in 3 patients because of side-effects and in 1 for a nonmedical reason).

† 1=1-1.9 months; 2=2.9 months; etc.

The patient who was reported to have died in diabetic coma was a 73-year-old man with diabetes of 18 years' duration. Tolbutamide therapy had been started on April 10, 1956, while he was at the New England Deaconess Hospital for treatment of cancer of the prostate. On June 21 he was transferred to another hospital for prolonged care and we did not see him again. At that time a blood sugar value of 92 mg. per 100 cc. was obtained. The diabetic condition appeared under excellent control with 0.5 Gm. of tolbutamide daily. He remained in the other hospital for over four months and was said during this time to have received 0.5 Gm. of tolbutamide daily. It was stated that, although on Nov. 16 a blood sugar value of 280 mg. was obtained, he was allowed to go home on a regimen of the same dosage of tolbutamide. However, readmission to the other hospital was necessary on Nov. 19 because of nausea and vomiting. It was stated that the patient had not taken tolbutamide and had eaten without regard to diet restrictions while at home. He was reported to have been in diabetic ketoacidosis; he was given 50 units of insulin, but died. No postmortem examination was carried out.

Factors Influencing Results of Tolbutamide Treatment

Age at Onset of Diabetes.—In figure 2 is shown the relation of age at onset of diabetes to the results secured with tolbutamide. It is noteworthy that, in the first three decades, there were relatively more failures than successes, as might have been predicted. In the decades 30-39.9 and 40-49.9 years, the ratio of number of patients with good results to those with primary failure was roughly 2:1. In succeeding decades, the ratio between good results and failures increased progressively. It must be kept in mind that the figure gives good results on selected patients. Tolbutamide trials were carried out much less commonly in patients below the age of 40 years than in those in older age groups.

Age of Patient at Time Tolbutamide Therapy Was Started.—It is evident from figure 3 that the number of patients with good and fair responses in the various age groups was relatively the same as those in whom primary and secondary failures were obtained. Therefore, the age of the patient at the time tolbutamide therapy was started is not of fundamental importance when one is dealing with subjects who are over 40 or 50 years of age. The important factor, as has just been brought out, is the age of the patient at the time diabetes had its onset, since in general the sulfonylurea compounds are effective in maturity-onset but not in growth-onset diabetes.

Duration of Diabetes at the Time Tolbutamide Therapy Was Started.—In figure 4 are shown the results of tolbutamide maintenance trials tabulated as to duration of diabetes. Two significant facts emerge: 1. The percentage of primary failures increased with increasing duration of diabetes. 2. Despite this trend, a significant number of patients with diabetes of 10 or more years' duration responded favorably. After consideration of these data with those shown in figure 2, it is reasonable to suppose that the successes in patients with long-term diabetes were, by and large, in those with onset above 40 years of age. Nevertheless, in this connection it is worthwhile to point out that, in dealing with subjects with maturity-onset type of diabetes, duration of diabetes need not be a contraindication to success with the orally given agent.

would be classified as unsatisfactory with respect to table 4. Consequently, it may properly be said that the sulfonylurea response test is only partly reliable in predicting good maintenance results. However, examination of figure 7 in the same way shows that, of 74 patients with primary failures, only 5 had satisfactory response tests in spite of the fact that many more than 5 had met the usual criteria for probable success with tolbutamide, such as older age at onset of diabetes and low insulin requirement. It is instructive that, among 70 patients who achieved fair control, about half (36) had sulfonylurea response tests earlier which were satisfactory and the other half unsatisfactory, thus taking a middle position between the well-controlled cases and the primary failures. Among 25 patients with secondary failures in whom response tests had been done earlier, 14 had had satisfactory and 11 unsatisfactory results with the response test.

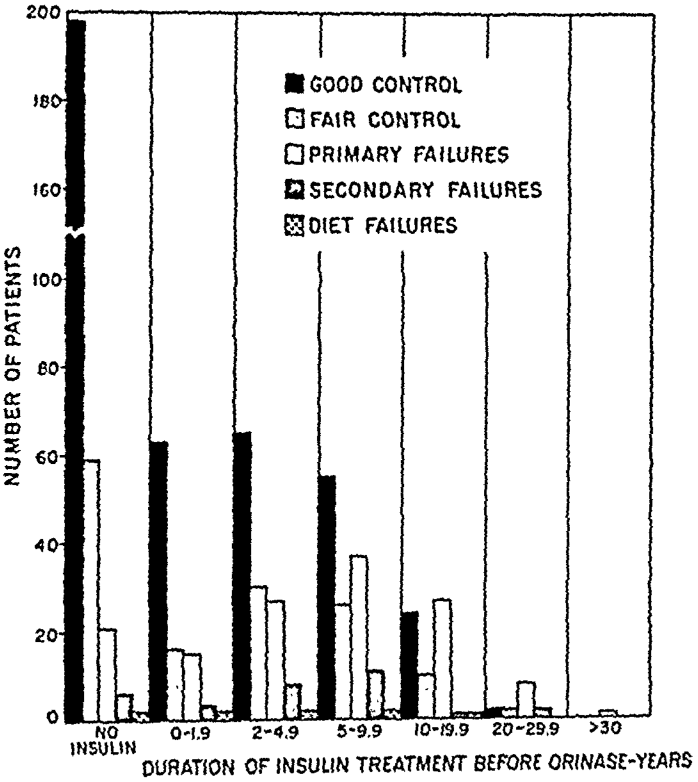

Fig. 6.—Correlation of duration of insulin therapy prior to use of tolbutamide with outcome of treatment with orally given agent.

In summary, the sulfonylurea response test affords a helpful, although by no means infallible, guide in the selection of patients most likely to respond favorably to drug therapy in day-by-day usage, gives enough security to start the treatment with nonhospitalized patients, and excludes cases in which it would be dangerous to stop treatment with insulin even for a few days. The test is quite reliable in predicting "primary failures," thereby avoiding the use of the drug in unsuitable patients. Moreover, a negative result has often helped to convince doubting patients that they cannot be treated successfully with tolbutamide. It is not as helpful in predicting "secondary failures," i. e., late failures in those patients who at first achieve good control.

If the results of the sulfonylurea response test are borderline or if on clinical grounds it seems reasonable to predict success on maintenance therapy, one may make a trial of day-by-day treatment. However, the patient should be kept under close supervision, with frequent tests of urine sugar and periodic determinations of the blood sugar level.

It is our custom on the day of the response test to have the patient, if an outpatient, wait until the blood sugar results are known. If the findings are favorable, a treatment schedule with tolbutamide is outlined; if unfavorable, insulin, if indicated, is given before the patient leaves and future treatment is planned.

Comment

The results just presented are those of a study of the effect of tolbutamide in 1,030 diabetic patients. After elimination of those with single dose tests only, those with insufficient data and those few treated with both tolbutamide and insulin, a total of 772 patients were left for consideration. Of these, 143 (17.6%) had "primary failures" with tolbutamide and consequent indication for treatment with insulin. Other small groups of patients having been discarded for various reasons, 594 patients were left for long-term study. It must be emphasized that, by this time, this group had become a rather highly selected one composed almost entirely of middle-aged and elderly persons with maturity-onset type of diabetes and with prior daily insulin dosage usually of 20 units or less. Among these 594 patients, long-term maintenance on tolbutamide therapy of 1 to 20 months resulted in good control of diabetes in 407 patients and in fair control in 143 patients.

From time to time, workers have reported as to the percentage of diabetic patients in whom hyperglycemia and glycosuria may be controlled with tolbutamide. Such percentages have meaning only when a statement is made as to the selection of patients used for tolbutamide trial. Although in selected groups of patients success may be achieved to an extent as great as 60 to 80% of subjects, if one considers all diabetic patients, a much lower percentage of the total can be treated successfully with the orally given agent.

It must be pointed out that, in the present study, the standards arbitrarily chosen for "good" and "fair" control are relatively strict as compared to those used commonly for patients maintained on insulin therapy. However, it has been our belief that, since the main advantage of the orally given hypoglycemic agents is that of convenience to the patient, truly good control should be insisted on if this type of treatment is to be followed instead of that with insulin. The hazard of hypoglycemia often prevents attempts at rigid control of diabetes with insulin. With tolbutamide, since significant and symptomatic hypoglycemia is rare, one can aim for normal blood sugar values without fear of undue depression of the blood sugar. Finally, analysis of data shows conclusively that, with respect to factors such as older age at onset of diabetes and lower insulin requirement as well as a satisfactory sulfonylurea response test, the patients who achieve good control are in a quite different class than those with fair control. This also lends weight to the feeling that probably tolbutamide therapy should not be continued for long periods in patients for whom only fair control can be achieved.

Indications for Tolbutamide Therapy.—It has been the experience of workers everywhere, beginning with the reports of German clinicians [14] as early as 1955, that the sulfonylurea compounds are effective in some middle-aged and elderly diabetic persons with a low insulin requirement. They are not effective in ketoacidosis and coma, during infections, or during and after many major surgical operations. They are not effective in children or in adults with the juvenile, unstable type of diabetes with an easy tendency to acidosis. Our experience agrees with these findings. The chief problem has been to attempt to find simple and workable criteria by which success or failure may be predicted among middle-aged and elderly persons with "mild" diabetes.

Analysis of our data indicates that success with tolbutamide in control of hyperglycemia and glycosuria is favored most in cases of maturity-onset type of diabetes and in cases of low insulin requirement. In other words, the drug works best in middle-aged and elderly diabetics who otherwise would take relatively small doses of insulin. Other favoring influences, discussed above, are short duration of diabetes and of insulin treatment; these are probably indirect factors.[14b] The sulfonylurea response test, already described, is also helpful in selecting patients in whom diabetes is likely to be controlled with tolbutamide therapy, provided a sliding scale of percentage fall in blood sugar level is employed.

Secondary Failures.—If the above considerations are kept in mind in choosing patients for tolbutamide therapy, there should be only a relatively small number of primary failures. However, the problem of "secondary" failures remains, i. e., the situation in which initial success in treatment over a period of at least one month is followed by "escape" from the effect of the drug with increase in hyperglycemia and glycosuria. Despite the fact that in our studies strict standards of control were used, a small number of secondary failures (including those due to lack of diet control) occurred—40, or 5.2% of the total. It must be acknowledged that further experience over a longer period of time may show a change in this regard.

The cause of the secondary failures is obscure. Critical analysis of results in our series of patients does not suggest that the cause was poor selection of patients or use of the wrong indications.[14b] In fact, in at least two-thirds of the patients with secondary failures, the influencing factors, such as results of the sulfonylurea response test, age at onset of diabetes, and the insulin dose, were the same as in those patients who have continued to the present to have satisfactory control with tolbutamide.

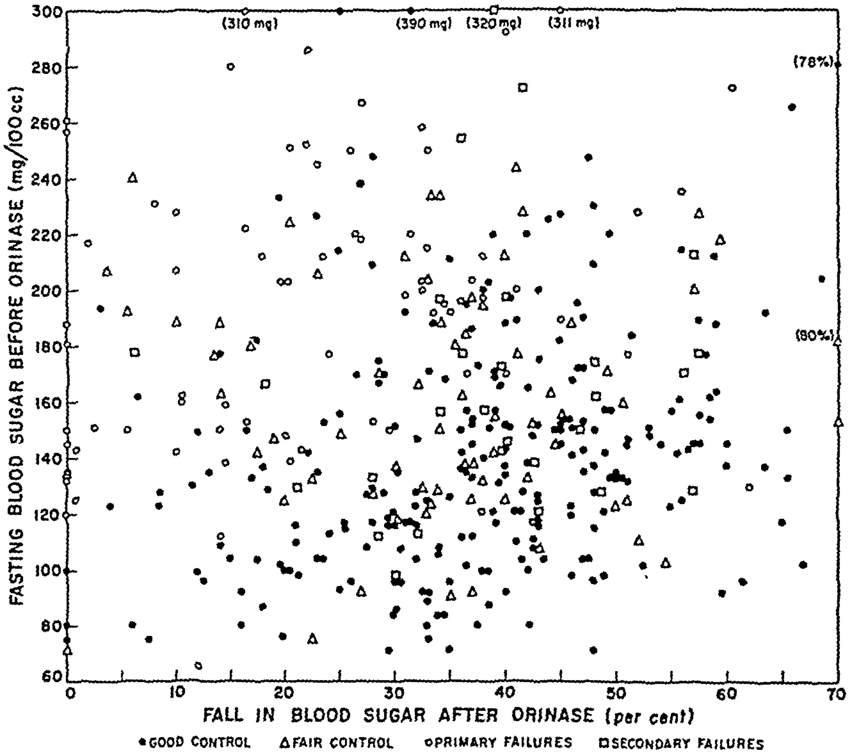

Fig. 7.—Correlation of fall in blood sugar level after single dose of tolbutamide and initial level of blood sugar with results of long-term treatment.

It has been suggested that in such patients a decreased capability for production of endogenous insulin has been brought about by prolonged stimulation with tolbutamide. As evidence in favor of such a view, some have reported [14b] that occasionally, on returning such patients to insulin therapy, the requirement has been significantly greater than before tolbutamide treatment. However, such has not been the experience in our patients. With the occurrence of secondary failures and return of patients to insulin therapy, the requirement has remained about the same as before. It must be pointed out that, in a situation such as this, the requirement for insulin after a period of poor control on tolbutamide therapy may well be somewhat higher than that in the same patient a few weeks later after a period of good control with insulin. Furthermore, entirely apart from tolbutamide, patients maintained on insulin therapy over extended periods of time often experience significant changes in insulin requirement.

Influence of Diet.—It should be emphasized that certain of the so-called failures with tolbutamide are in reality due to failure of the patient to follow diet instructions. Lack of adherence to diet affects, of course, the results of treatment with insulin, but with tolbutamide other considerations are evident. Some patients receiving medication orally instead of by injection may not be so impressed with the existence of diabetes and the necessity of following a diet. Furthermore, dietary indiscretions may be counterbalanced to some extent by administration of a larger dose of insulin, whereas with tolbutamide increase in dosage will not allow an increased food intake. Regardless of other considerations, there is no doubt but that the introduction of the orally given hypoglycemic agents has called attention anew to the fundamental and striking value of a restricted diet in the treatment of diabetes.

An occasional patient receiving tolbutamide may experience such an increase in carbohydrate tolerance that, with reduction in dosage of the drug to only 0.5 Gm. daily, the urine remains consistently free from sugar and blood sugar values are well within normal limits regardless of time of day or relation to meals. In such patients, the indication is to omit tolbutamide entirely. In certain of these patients, one will find that even without tolbutamide, normoglycemia and aglycosuria persist. In such instances doubt may be raised justifiably as to whether tolbutamide therapy should have been started in the first place. Indeed, this situation emphasizes the point that patients with "mild" diabetes, particularly if obese, should be treated at first with diet restriction alone, since in many cases remarkable improvement may be expected. However, it would appear likely that many patients at first require and benefit from tolbutamide, in addition to diet restriction, and improve after a period of time so that the drug is not necessary later. In these patients, however, it may be necessary at a later date to return to tolbutamide therapy.

Special Advantages of Oral Treatment.—The chief advantage of the orally given hypoglycemic agent is that of convenience. Consequently, in any patient in whom the indications for such management are questionable or in whom the results after trial of the orally given compound are poor, insulin should be used without hesitation and without delay. However, the convenience of treatment by mouth as opposed to treatment by injection appeals to all persons. It is particularly welcome to blind patients, to those with disabilities or tremor of the hands, and to those who are highly nervous. In this connection, there should be recorded our experience that many patients "feel much better" on therapy with tolbutamide than with insulin. This impression is, of course, greatly influenced by emotional factors such as relief from the necessity of injections and freedom from worry regarding insulin (hypoglycemic) reactions. One must confess that at times such patients may return for examination with significant hyperglycemia and glycosuria, with lack of correlation with degree of control of diabetes and sense of well-being. This experience emphasizes that patients receiving tolbutamide must be seen regularly and blood sugar determinations done at sufficiently frequent intervals to insure that the diabetes is kept under good control.

One might postulate a special benefit in those who are allergic to insulin. However, tolbutamide treatment is not successful in many such patients because of the nature of the diabetic state and a high insulin requirement. Furthermore, even in those in whom tolbutamide treatment yields satisfactory results, one must keep in mind the possible need for insulin in the future at times of emergency. Certainly if in any given patient such seems at all likely, it is wise to carry out desensitization to insulin and to use insulin rather than tolbutamide in treatment.

Hypoglycemia.—In addition to convenience, treatment with tolbutamide has the added advantage of almost complete freedom from significant hypoglycemia. In our series of well over 1,000 patients given tolbutamide at one time or another, in only a very few instances was symptomatic hypoglycemia recognized, despite the fact that most adult patients at the start were given a full dose of 3 Gm. in the fasting state, with food being withheld for four hours in order to carry out the tolbutamide response test. The case of one patient with symptomatic hypoglycemia is given below.

A thin, frail woman, 74 years of age, with diabetes of eight years' duration had been admitted to the hospital after a cerebral thrombosis with right-sided hemiparesis. Since discovery of diabetes she had taken a small dose of insulin daily; most recently this had been 8 units of the protamine zinc type daily before breakfast. On Aug. 8, 1957, a sulfonylurea response test was carried out after a day during which no insulin had been given. The fasting blood sugar level was 83 mg. per 100 cc. After 3 Gm. of tolbutamide was administered, the blood sugar level in two hours had fallen to 68 mg., and in four hours to 50 mg. per 100 cc. During most of the day the patient complained of malaise and appeared a bit dull. However, symptoms were mild and she carried through the day without particular incident. The following morning there was difficulty in arousing her. Hypoglycemia was suspected and blood drawn for sugar determination. After this, she was given orange juice with some difficulty and she promptly revived. When the blood sugar value was reported it was stated to be 38 mg. per 100 cc. She was placed on therapy of 0.5-1.0 Gm. of tolbutamide daily, and in February, 1958, at a hospital stay her diabetic condition was found to be under excellent control.

The incidence of marked, prolonged, or symptomatic hypoglycemia after treatment with tolbutamide has been so low that we believe hospitalization is not necessary for initiation of treatment, even on the test day on which a full dose of 3 Gm. is given at one time. Furthermore, the almost entire freedom from danger of hypoglycemia, particularly on maintenance doses of 0.5 to 2.0 Gm. of tolbutamide, may make it possible for patients to engage in those occupations in which potential hypoglycemia has been considered disqualifying.

Summary

Tolbutamide (Orinase) was used in treatment of 1,030 diabetic patients. In 772 of these, treatment with tolbutamide was begun and, at the time of completion of the study, had been carried out for 1 to 20 months in 594 patients. Good control of hyperglycemia and glycosuria was obtained in 407 (52.6%) and fair control in 143 (18.5%) of this selected group of 772 patients. The incidence of failures was as follows: "primary," i. e., within the first month of treatment, 136 patients (17.6%); "secondary," 31 patients (4%); failures due to disregard of diet, 9 patients (1.2%). In 33 patients (4.3%) the drug had been used for less than one month; in 8 (1.1%) treatment with tolbutamide was stopped because of toxic side-effects; and in 5 (0.6%) the treatment was discontinued for nonmedical reasons.

Factors favoring success with tolbutamide were primarily maturity-onset type of diabetes (onset usually above the age of 40 years) and a low insulin requirement (less than 20 units daily). A single-dose, four-hour sulfonylurea response test was found to be of value in pointing out those patients in whom primary failure with tolbutamide therapy is likely to occur.

Untoward effects were low in incidence and in general consisted chiefly of urticaria and minor digestive disturbances. In one patient with cirrhosis of the liver, jaundice occurred three months after beginning treatment with tolbutamide; the relation of jaundice to the drug is uncertain. In two patients dying of causes unrelated to tolbutamide administration, histological examination revealed no evidence of damage to the pancreas or liver which could be attributed to the drug.

In the selection of patients to be treated with tolbutamide, care should be taken to avoid, on the one hand, unnecessary use in those with whom dietary restriction will suffice and, on the other hand, unwise use in those requiring insulin for maintenance of control of diabetes.

15 Joslin Rd. (15) (Dr. Marble).

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USE OF HOOKPLATE FOR FIXATION OF UNUNITED MEDIAL TIBIAL MALLEOLUS

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Nonunion of the medial tibial malleolus is one of a group of fractures for which there is no satisfactory method of internal fixation. Most of the difficulties can be overcome by the use of the hookplate here described. Made of malleable stainless steel in several sizes, it can be adapted closely to the contours of the bone structure. The hookplate fixation has been successfully used in over 350 cases representing fractures of the medial or lateral malleolus, comminuted or malunited malleolar fractures, olecranon fractures, especially if they were comminuted, and fractures in several other locations in the body. Usually these fractures represent a part of a joint, which is of great importance for structural stability and/or attachments of ligaments and tendons. In applying it, care is taken to preserve the articular surface of the bone and to achieve, if possible, a stable hairline reduction of the malleolar fragment so as to restore the normal ankle mortise. Also, the hookplate fixation allows a type of bone grafting procedure described and illustrated in this paper, which is technically not difficult. Ten fractures, one of which is described in some detail, have been treated with excellent anatomic and functional results.

The surgical treatment of nonunion of the medial tibial malleolus still presents a technical problem which has been given only scant consideration in literature and textbooks.[1] It is simply stated that in case of nonunion the fracture site should be freshened, a screw or wire should be used for fixation, and some type of bone graft should be applied.

Kelikian [2] describes a slightly different method in which an intramedullary bone graft is used and fixation obtained with two wire sutures. It is felt that these methods lack the degree of fixation for the small fragment which is desirable in order to obtain consistently good results. Therefore, a method is suggested which has been successfully applied in 10 cases of nonunion of the medial malleolus.

Principles of the Method

Fixation is obtained by means of a hookplate (fig. 1), commercially available in different sizes, which can be applied without any technical difficulty and which permits associated intramedullary or other types of bone grafting. The hookplates are of stainless steel, malleable, and can readily be shaped to conform to bony contours.

In the German literature, several authors [3] report favorably on the use of the hookplate. Lange[4] enumerates the different methods for fixation of the fractured medial malleolus and summarizes the advantages with the use of the hookplate. He states that the two hooks grasp the fragment firmly, eliminate the displacing force transmitted through the deltoid ligament, and provide reliable fixation to the tibia. Witt [5] stressed the same points in discussing the treatment of the fractured medial malleolus as either a fresh fracture or a pseudarthrosis.

It should be emphasized that not all patients with nonunion of the medial malleolus need surgical repair. In one group either the condition is asymptomatic and requires no treatment, or the fracture can be controlled by conservative measures or simple excision of the distal malleolar tip. It is the second group which usually experiences a progressive amount of pain on physical activity and requires reconstructive surgery.

In the typical case of nonunion of the medial malleolus, we find on the roentgenogram a rarefied line of bone defect surrounded by some sclerotic bone. The blood supply of the distal fragment depends on the level of the fracture. If it is a typical inversion type of fracture, evidenced by an oblique fracture line extending proximally toward the tibial shaft, the main blood supply to the fragment through the anterior tibial artery may still be intact. If it is the transverse type of fracture line (eversion type) at the level of the tibial joint surface or distal to it, this main blood supply is interrupted and the only vessels which remain are those reaching the fragment through ligamentous structures. This important aspect of the blood supply, which has been stressed by Kelikian, should be remembered at the time of surgery and preserved accordingly. Our aim is to reduce the fracture as exactly as possible after excision of the area of pseudarthrosis, retain all possible blood supply, obtain rigid fixation, and apply some type of bone graft.

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Surgical Procedure

The skin incision and subperiosteal exposure of the pseudarthrosis are performed in routine manner, extending proximally on the tibia sufficiently to allow the placement of the hookplate. The pseudarthrosis is excised, and the fragments are freshened down to cancellous bone. If the distal fragment is sclerotic, one will be unable to expose cancellous bone and must be satisfied with less suitable bone structure. Precaution is taken to preserve the articular surface. An attempt should be made to obtain a hairline reduction of the malleolar fragment to restore the normal ankle mortise. Occasionally, a portion of the anterior and posterior ligamentous attachments have to be severed, and the heel must be adducted to allow an accurate reduction. The main portion of the deltoid ligament, however, must be preserved.

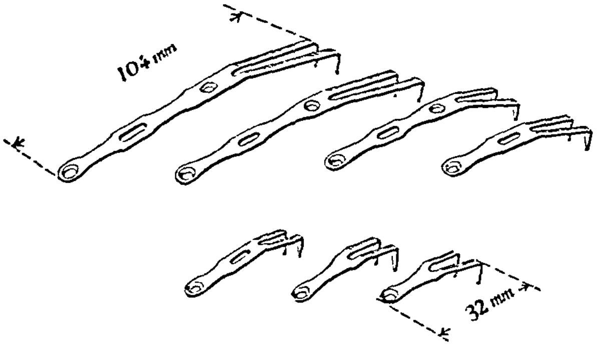

Fig. 1.—Hookplates from 32 to 104 mm. in length. Smaller ones have only one hole, whereas larger ones have two or three holes, one of which is enlarged to a slot to permit further impaction before screw is tightened.

By means of a Kirschner wire, two holes are drilled into or close to the tip of the malleolus. The holes are directed obliquely toward the fracture site (fig. 2, *A* and *B*) and are about 8 to 12 mm. apart, depending on the size of the malleolar fragment. The drill holes should not enter the joint and should remain inside the cancellous portion of the bone. A two-hole or three-hole hookplate is selected, depending on the size of the fragment and the force which is required to maintain reduction. In order to obtain maximum stability, a three-hole hookplate is preferred. This is in contrast to fresh fractures, which usually require only a small one-hole hookplate 32 mm. in length.

The hookplate and its prongs are bent with small pliers to conform to the bony contours of the fracture site, after which the hooks are introduced into the prepared holes and lightly impacted. Final adjustment of the shape of the hookplate can be made before the hooks are fully impacted. While the fracture is held tightly reduced by an assistant, with close contact of the hookplate to the bone, the first drill hole is made through both tibial cortices at the proximal end of the slot, followed by introduction of the screw. Prior to tightening of this screw, the fragment is again snugly approximated by the assistant. A screw is then inserted through the distal hole of the plate penetrating only one cortex in order to avoid the joint. Finally, the second bicortical screw is applied through the proximal hole in the plate. This completes the first part of the procedure and results in solid fixation of the fragment.

The second step is the bone grafting procedure. The following method has been found to be simple and rewarding. Directly behind the posterior prong of the hookplate and in front of the anterior prong, grooves 6 to 8 mm. in width and 15 to 20 mm. in length are made in the cortex of the tibial shaft. With these grooves as guides, drill holes are then made into the malleolar fragment (fig. 2). Two cancellous-cortical bone grafts of appropriate size to fit the drill holes are obtained from the wing of the ilium. These are introduced obliquely into the

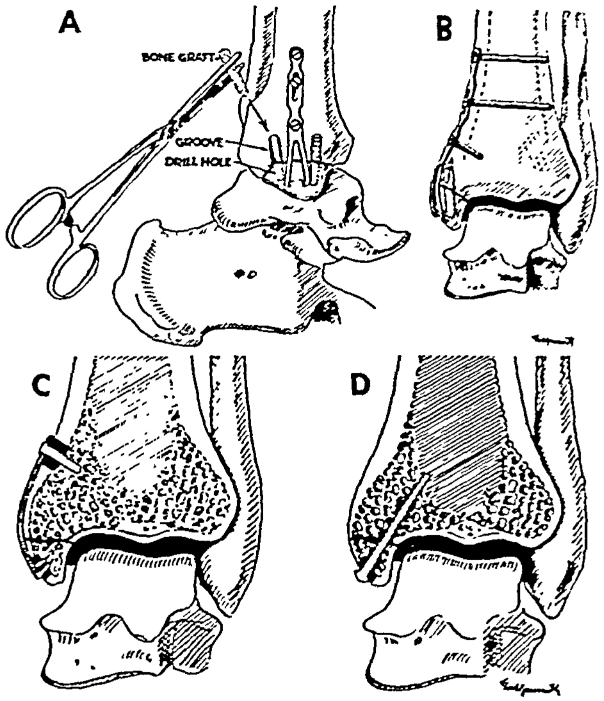

Fig. 2.—*A* and *B*, surgical procedure for nonunion of medial malleolus, illustrating solid fixation obtained with hookplate and bone grafting by cortical and cancellous pegs from wing of ilium. *C*, principle of hookplate fixation. Fragment is grasped by two hooks while screw rests securely against cortical type of bone in transverse direction to force of distraction. Screw and hooks are directed slightly towards fracture site in order to obtain firm grasping force. *D*, method of direct screw fixation in which screw engages only cancellous bone and in line of force distraction.

two holes and are then impacted into the grooves. Additional cancellous material is used to fill the space around the grafts. If necessary, further grafting can be accomplished by a bone onlay over the fracture site. The wound is closed in layers beginning with the periosteum, and a long leg plaster is applied.

Postoperative Care

The plaster is changed after 14 days, and the sutures are removed. At the end of six weeks, a short leg plaster is applied until bone healing is demonstrated by roentgenogram. This usually occurs on an average of eight weeks after the operation. Foot and ankle exercises are begun at this time. Graduated weight bearing is started at 10 weeks, but full weight bearing is not permitted for an additional 2 weeks. Ten patients have been treated by this method. The following case is representative.

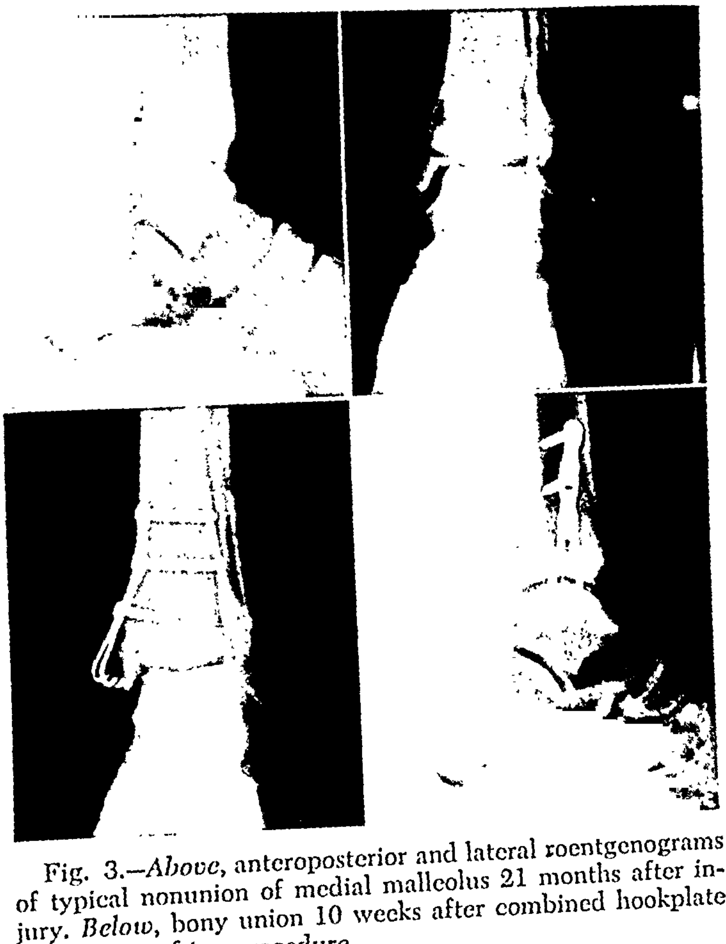

Fig. 3.—*Above*, anteroposterior and lateral roentgenograms of typical nonunion of medial malleolus 21 months after injury. *Below*, bony union 10 weeks after combined hookplate and bone grafting procedure.

Report of a Case

This patient, aged 20, fractured his medial malleolus in January, 1955. He was treated by closed reduction and immobilization in plaster. He was returned to duty about 10 weeks later with a definite nonunion. On Oct. 22, 1956, he twisted the same ankle severely while playing football and immediately developed pain over the old fracture site. It was decided, because of the patient's youth and desire for full athletic activity, to operate in order to obtain bone union. On Nov. 1, 1956, the patient was operated on by the method described above. There was eight weeks of postoperative immobilization followed by graduated weight bearing two weeks later. This patient was returned to duty on Jan. 23, 1957, 12 weeks after surgery, with no discomfort and with roentgenographic evidence of bone union (fig. 3).

Salient Points of the Method

1. The hookplate gives solid fixation of the fractured medial malleolus, regardless of size and shape. Screws and wires still allow distraction and rotation of the fragment if not well engaged proximally inside the tibia. Venable and Stuck[6] state, "No screw holds well in cancellous bone." To engage the opposite cortex of the tibia would require a rather long screw (fig. 2, *C* and *D*).

2. The metal does not enter the fracture site itself but surrounds it from the outside. This preserves all cancellous bone for contact with the intramedullary bone graft. A screw inserted into the malleolus replaces some cancellous bone material, and its position must be checked by roentgenograms to rule out possible encroachment of the joint itself. Once a screw has been introduced, any further adjustment which may be required will endanger the rigid fixation which is so desirable.

3. There is minimal damage to the remaining blood supply of the malleolar fragment by avoiding the insertion of a screw through the tip of the malleolus. This is the point of attachment of the ligamentous structures which contain important vascular elements.

4. In contrast to screw fixation, the hookplate is effective in the presence of osteoporotic bone and does not split the fragment.

5. Because of the solid type of fixation, prolonged plaster fixation is not required, and early mobilization without weight bearing can be encouraged.

6. The hookplate, which is commercially available in different sizes, can be bent easily to conform to the contour of the bony structures and is well tolerated by the overlying skin.

7. I have not observed structural weakness of the commercially available hookplates if they are properly introduced after a hairline reduction has been obtained. It should be stressed again that the hooks have to be introduced into prepared holes; otherwise, they frequently will straighten out and not engage directly the small fragment. This experience contrasts with that in one report which indicates structural weakness with loss of the desired solid fixation allowing renewed displacement. Still, this criticism has to be taken seriously, and every effort should be made to standardize the quality of the material by the manufacturing companies.

Comment

Many different gadgets have been described for fixation of fractures of the shaft of the long bones and of the neck of the femur (screws, plates, slotted plates, bands, wires, and intramedullary nails). Very few, however, have been developed for fixation of a small bone fragment which is either important for structural joint stability or is essential for ligamentous attachment. One might, therefore, conclude that none is needed. Wire or screw fixation may give satisfactory results, but there are a number of conditions which cannot be treated adequately by these conventional methods. It is felt that the hookplate fills a definite need and enables the surgeon to deal successfully with this group of fractures for which there is no satisfactory method of internal fixation. *Nonunion of the medial tibial malleolus* may be classified in this latter group. Ten such cases have been treated successfully with the hookplate, and bony union resulted in all of them within 10 weeks. The functional results, of course, do not depend entirely upon the bony union of the medial malleolus, but this aspect of the injury was dealt with successfully in every case.

In evaluating the technical aspect of this method of fixation, it should be stated that this report on the hookplate is not based on these 10 cases alone but on over 350 other cases in which patients have been treated during the past 10 years in a similar way.[7] This method has given consistently reliable fixation of small bone fragments with an extremely high rate of bone union. No displacement of the fragment has been observed such as is occasionally seen with other types of fixation. The hookplate has been applied for (1) fresh or recent fractures of the medial or lateral malleolus, (2) comminuted fractures of the medial malleolus, (3) malunited medial malleolar fractures, (4) comminuted olecranon fractures, (5) fixation of small fragments of other joints (knee, shoulder, and hip), and (6) fractures of the distal tibial epiphysis.

The objection to the hookplate which has been raised by Riess,[8] Buck-Gramcko,[9] and Fackert [10] is based on the requirement for broader exposure and more extensive surgery than with some other methods. This seems unjustified, since in none of my 350 cases was there any breakdown of the surgical wound or the overlying skin. In order to accommodate the hookplate, the incision must be extended proximally 1 or 2 cm. more than is required for simple screw fixation. No harmful effect of any kind has been observed from this added length. It should also be noted that the introduction of a screw in a very oblique direction to avoid encroachment on the joint requires a longer distal incision than is customary with the use of the hookplate. In all cases the hookplate has enabled me to deal successfully with the fixation of small fragments, regardless of their size, shape, or bony consistency.

Summary

The hookplate has been used as a method of treatment for nonunion of the medial tibial malleolus. Ten fractures have been treated, with excellent anatomic and functional results. This method has certain advantages over other forms of internal fixation.

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RETROSTERNAL PLACEMENT OF ASCENDING COLON FOR ESOPHAGEAL SUBSTITUTION

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and
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Reestablishment of continuity of the passage from pharynx to stomach after removal of a diseased esophagus, or in the absence of the esophagus, formerly depended on the use of external tubes constructed of skin, stomach, or small intestine. These have been unsatisfactory for various reasons. Since 1951 it has been possible to reestablish the connection of pharynx to stomach by a retrosternal segment of colon within the thorax. Three cases are described illustrating the usefulness of this procedure in three types of esophageal disease. In one patient, a 64-year-old man, carcinoma had infiltrated most of the esophagus, and a previously unsuspected fungating carcinoma was found in the stomach at operation. The substitution of a segment of colon for the esophagus was successfully carried out, and the transplanted colon functioned well for six months until death. Substitution of colon for esophagus likewise succeeded in an 11-year-old girl with esophageal stricture after the ingestion of lye, and in a 3-year-old boy born with complete atresia of the esophagus. In both children subsequent growth has been normal. This type of operation is recommended particularly for benign lesions of the esophagus in which long-term survival is anticipated.

The surgical management of congenital and acquired lesions of the esophagus presents unusual problems not common in other forms of surgical therapy. Nearly half a century has elapsed since Torek [1] reported the first successful resection of the thoracic esophagus. External tubes were used to replace the esophagus. Many methods used since that time for the reestablishment of continuity after partial or complete resection of this organ have not proved entirely satisfactory. This is particularly true after esophageal resection for benign lesions, after which long-term survival is anticipated. Recent experiences in which an isolated segment of colon is used to replace the esophagus suggest that this method may be preferable in many instances to those heretofore employed.

The employment of segments of colon for esophageal substitution is not new. A successful case was reported by Kelling [2] as early as 1911 and the advantages of using part of the colon as a subcutaneous esophagus were discussed by Vulliet [3] in the same year. Von Hacker [4] reported the successful use of this method in 1914. Orsoni and Toupet [5] described the first case in which a segment of colon was carried as high as the neck through a subcuneous tunnel in 1950. Scattered reports of similar procedures have appeared in the European literature.

Replacement of the esophagus by a part of the colon within the thorax was first described by Rudler [6] in 1951. He placed a segment of ascending colon and ileum retrosternally as a palliative procedure in a patient with carcinoma of the esophagus. Lortat-Jacob [7] used a segment of ascending and transverse colon in the same year for a case of lye stricture of the esophagus. The distal end of the colon segment was anastomosed to the jejunum in both instances. In 1952, Robertson, Howe and Smithwick [8] reported a successful case of esophageal substitution in which the transverse colon was interposed between the esophagus and jejunum. Kergin,[9] in 1953, employed a staged procedure in the insertion of a segment of transverse colon to bypass a high esophageal obstruction due to mediastinal paraffinoma. Battersby [10] reported an experimental and clinical study in 1953. Additional patients with carcinoma of the esophagus so treated were reported by Mahoney and Sherman [11] in 1954. Dale [12] and Sherman [13] utilized segments of ascending colon in three patients with esophageal atresia and in two additional patients with carcinoma of the esophagus in 1955.

Replacement of the esophagus by segments of colon, especially for benign lesions, may prove superior to other procedures for several reasons. The colon is more resistant to acid gastric secretion than the jejunum or the esophagus itself.[14] Reestablishment of esophageal continuity can therefore be accomplished without the need to bypass the stomach. A sufficient length of viable colon is easily mobilized for even the highest anastomosis in the neck. The adequacy of the blood supply may be determined prior to mobilization of the colon by the observation of the colon during application of vascular clamps to the vessels requiring ligation. In some cases, sufficient length is obtained so that the cecum, the ileal stump, and the appendix can be safely removed, thus eliminating two of the suture lines. This was possible in two of our patients. Adequate preoperative preparation with neomycin and other agents is probably helpful.

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It seems worthwhile to report our experience with three consecutive patients in whom isolated segments of colon were used to replace the esophagus. These three patients, one of whom had carcinoma of the esophagus, one congenital absence of the esophagus, and one lye stricture of the esophagus, illustrate the variety of esophageal lesions that may be treated by this method.

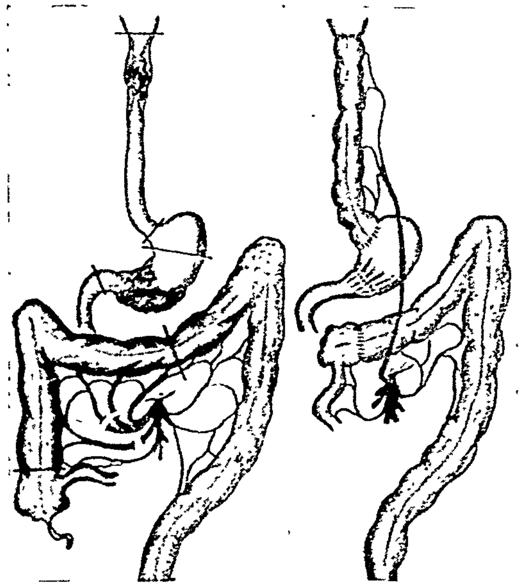

Fig. 1 (case 1).—Lesions, vascular pattern, and reconstruction.

Report of Cases

Case 1.—A 64-year-old man was admitted to Jefferson Medical College Hospital on March 23, 1956, with a history of progressive dysphagia for six months. He had lost 35 lb. (15.9 kg.). Barium swallow revealed the esophagus to be almost completely obstructed by an infiltrating lesion beginning 3 cm. below the larynx.

Operation was performed on March 30, 1956. A cervical and an anterior thoracotomy incision, both on the right side, were used to mobilize the proximal and thoracic portions of the esophagus. The abdomen was then opened through a midline incision, and a previously unsuspected fungating carcinoma of the stomach was found. A radical subtotal gastric resection was carried out and a Billroth 1 type of anastomosis performed. The ascending and transverse colon were then mobilized. Three middle colic arterial branches were present. It was necessary to divide the right colic artery and two right-middle colic arterial rays. The colon was divided just distal to the cecum and again just distal to the midtransverse colon. The single remaining middle colic artery provided an adequate blood supply for the entire colonic segment, which was brought up to the neck through a retrosternal tunnel and anastomosed to the pharynx and the gastric fundus. Colonic continuity was reestablished by a colocolostomy. In this case the total esophagectomy and radical subtotal gastrectomy were well tolerated by the patient. The postoperative course was uneventful except for a single episode of atelectasis of the right lung, which was treated by two bronchoscopic aspirations. The patient was discharged on the 15th postoperative day able to eat a full diet. The histological diagnoses were (1) poorly differentiated squamous cell carcinoma of the esophagus and (2) adenocarcinoma of the stomach, intermediate grade.

The patient died in September, 1956, six months after operation, in another hospital. Postmortem examination revealed cerebral metastasis, but it is not known whether this was secondary to the esophageal or to the gastric carcinoma. The patient had clinical evidence of other distant metastases. He obtained excellent palliation, and the transplanted colon functioned well until his death.

Comment.—It was fortunate that the colon was prepared with antibiotics in this case. Had the colon not been so prepared, it is unlikely that continuity could have been easily reestablished by other means after a radical subtotal gastric resection. Anatomic variation in the midcolic artery in this patient is shown in figure 1. In cases of esophageal carcinoma in which the lesion cannot be removed, bypass alone can provide palliation.

Case 2.—A boy was born on March 2, 1953, with complete atresia of the esophagus. Twenty-four hours after birth a pharyngeal fistula was established on the left and a gastrostomy performed in another hospital. The child was fed through the gastrostomy and at the same time encouraged to swallow foods in order to establish the swallowing reflex.

On Nov. 5, 1956, the patient was admitted to Jefferson Medical College Hospital for consideration of esophageal reconstruction. Roentgenographic examination revealed no distal esophageal segment. On Nov. 16, 1956, the patient was operated on under general anesthesia. The ascending colon was mobilized through a midline abdominal incision. Two midcolic arterial branches were found. The right midcolic branch and the ileocolic arteries were divided. The terminal ileum was divided and its distal stump inverted. The transverse colon was divided just to the left of the midcolic artery. An ileotransverse colostomy was then carried out. The pharyngeal fistula was mobilized through a left transverse cervical incision. The pharynx was extremely thin and attenuated. A tunnel was made in the retrosternal space and the colon was rotated so that the appendix, cecum, and terminal ileum were delivered through the lateral cervical incision. Because of the length of colon obtained it was possible to amputate the colon distal to the cecum and remove the cecum, terminal ileal stump, and appendix. The colon was then anastomosed to the pharynx and stomach and the wounds closed (fig. 2).

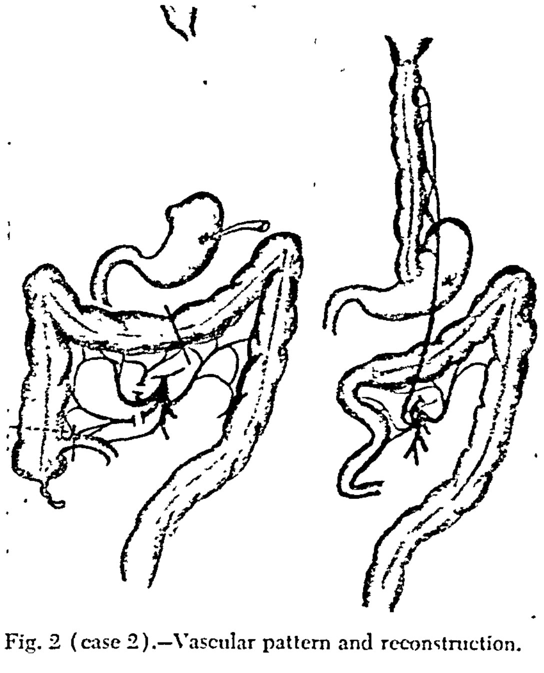

Fig. 2 (case 2).—Vascular pattern and reconstruction.

The postoperative course was uneventful, and the patient was discharged two weeks after the operation. The x-rays are shown in figure 3. The patient was eating a full diet on the eighth postoperative day, and the gastrostomy tube remained clamped until its removal two months later. The patient was seen on Sept. 26, 1957, and remains asymptomatic. There is no difficulty in swallowing, and he can eat a full diet. His growth and nutrition are normal.

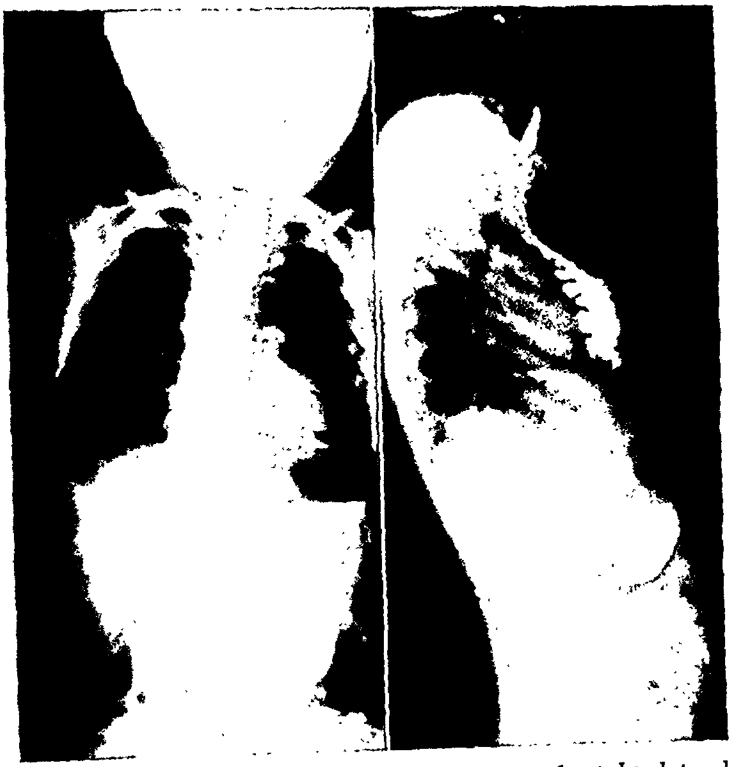

Fig. 3 (case 2).—*Left,* anteroposterior and, *right,* lateral postoperative barium swallow x-rays.

Comment.—This is an example of substitution of the colon for a congenitally absent esophagus. It was interesting to note that the pharyngeal wall was extremely thin and attenuated, perhaps the result of lack of resistance to the contraction of the pharyngeal musculature. A different anatomic variation of the midcolic artery was found in this patient.

The gastrocolonic anastomosis was performed on the lesser curvature of the stomach with the consideration that should peptic colitis develop a proximal gastrectomy could be performed more easily. Resection of the vagi was not required in this case, so that a decompression gastroenterostomy, pyloroplasty, or pyloromyotomy was not necessary.

Case 3.—An 11-year-old girl was admitted to the Jefferson Medical College Hospital for the fourth time on Oct. 23, 1956. She had had an extensive stricture of the entire thoracic esophagus after the ingestion of lye six years previously. A gastrostomy was performed at that time and she was treated with periodic esophageal dilatations for three years. She was then readmitted because of pneumonitis and failure of dilatation to provide an adequate esophageal lumen. A thoracotomy was performed on the left and esophageal dilatation carried out under direct vision. This operation was complicated by postoperative staphylococcic abscesses in the left lung and empyema on the left. The child recovered slowly, and an adequate nutritional status could be maintained by esophageal bougienage and gastrostomy feeding. Despite repeated esophageal dilatations she again developed dysphagia and was readmitted for consideration of esophageal bypass. On Nov. 19, 1956, the patient was again operated on. The proximal esophagus was exposed and mobilized through a right oblique cervical incision. It was divided and the distal segment closed. The abdomen was opened through a paramedian incision on the right, and the ascending and transverse colon mobilized as previously described. A single midcolic artery was present. The distal ileum was divided and its stump inverted into the cecum. The transverse colon was divided to the left of the midcolic artery and an ileotransverse colostomy carried out. The cecum and ascending colon were brought up to the cervical incision through a tunnel behind the sternum. The appendix was removed and the greatly hypertrophied proximal esophageal segment anastomosed to the cecum. The distal end of the transplanted colonic segment was anastomosed to the stomach (fig. 4). Her postoperative course was uneventful, and when discharged she was eating a full diet without difficulty. On Dec. 13, 1956, the gastrostomy was closed, and she has since remained completely asymptomatic.

Comment.—This case presents an example of colonic substitution of the esophagus for an acquired benign lesion. Vagotomy was not necessary in this patient, and therefore a gastric decompression operation was not required. She has obtained an excellent result after years of unsuccessful esophageal dilatation and continues to eat a full diet without symptoms.

A third variation of the midcolic artery was present. The extreme hypertrophy of the proximal esophageal segment in this patient was interesting. It was probably the result of swallowing against the resistance provided by the esophageal stricture.

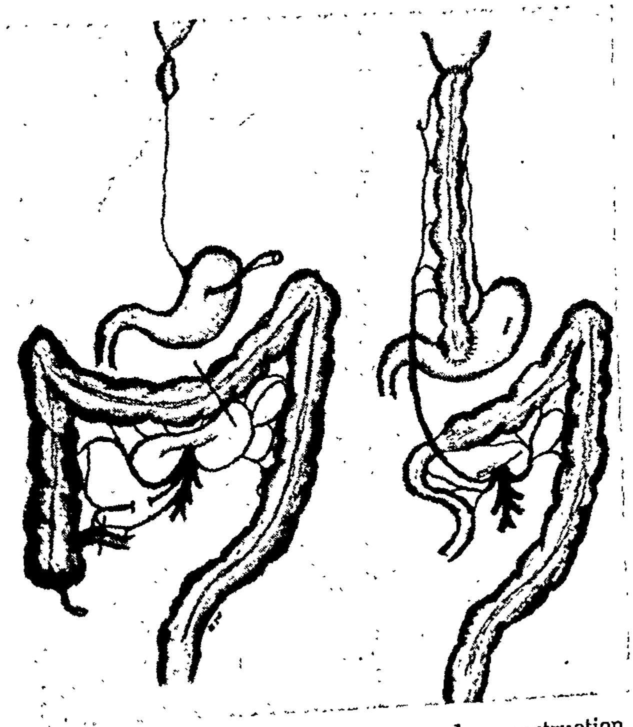

Fig. 4 (case 3).—Vascular pattern and reconstruction.

Summary

Three successful consecutive esophageal substitutions by retrosternal transplantation of the colon were performed, one for carcinoma of the esophagus, one for congenital absence of the esophagus, and one for acquired stricture of the esophagus. In each instance the patient obtained an excellent functional result from the operative procedure employed, and no serious difficulties were encountered in the postoperative period.

No evidence of peptic colitis was noted during the follow-up period of 6 months in one and 11 months in two patients. We suggest that isolated colonic segments be utilized for esophageal substitution more frequently. This technique is recommended particularly for benign lesions of the esophagus in which long-term survival is anticipated.

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USE OF ARTIFICIAL KIDNEY.—The terminal stage of acute uremia, characterized by coma, convulsions or severe cardiac failure, is not the best possible time for dialysis, even though some patients can yet be saved at this late stage of the artificial kidney. . . . It is not often realized . . . that (*a*) terminal stages are often not reversible with or without dialysis, (*b*) preterminal stages frequently deteriorate within a matter of hours into terminal stages, and (*c*) irreversible (or slowly reversible) injury to nervous or circulatory systems can occur early (before the 10th day) in the course of acute anuria. It has been proposed that a skilled and experienced physician is able to postpone dialysis or avoid it entirely. One should receive this argument with the utmost skepticism, inasmuch as it is unsupported by evidence. . . .

I . . . favor initial hemodialysis (*a*) whenever necessary for electrolyte abnormality; (*b*) if there are any clinical signs, on the fifth day of anuria-oliguria; (*c*) if there are no clinical signs but continuing oliguria on the sixth day; (*d*) thereafter, repeat dialysis whenever indicated clinically or by serum electrolytes or by BUN over 150. If we had adopted a rule to dialyze all patients who remain anuric for five or six days, we would have dialyzed an additional six patients who recovered without the use of the artificial kidney and where this treatment would have been superfluous. We would also have dialyzed 16 of the 17 patients in whom the artificial kidney was applied too late, with an unknown and unknowable, but probably very considerable, salvage. In view of the very small risk, the conclusion is inescapable that early use of the artificial kidney would have been preferable in the present series of patients.—P. F. Salisbury, M.D., Ph.D., Timely Versus Delayed Use of the Artificial Kidney, *A. M. A. Archives of Internal Medicine*, April, 1958.

POSTHEMIPLEGIC REFLEX SYMPATHETIC DYSTROPHY

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Hemiplegia in the six cases here described was followed by a painful syndrome in the affected upper extremity. Progressive changes were observed in soft tissues, joints, and bones. Ipsilateral stellate ganglion blocks afforded prompt but not always permanent relief, and the two patients who submitted to high thoracic sympathectomy obtained lasting benefit. The evidence showed that much of the disability represented inhibition caused by severe pain and trophic changes. The prompt remission of the symptoms after sympathetic block or sympathectomy enabled the patient to utilize powers still latent in the extremity and greatly facilitated the program of rehabilitation.

Multiple complaints referable to the extremities are frequently encountered during the rehabilitation of patients with cerebral lesions, particularly cerebral vascular accidents. These symptoms may often prevent the successful completion of a rehabilitation program. Many of these patients have a relaxation of the shoulder capsule associated with pain, due to traction of the paralytic extremity. In these patients, Tobis[1] has recently recommended the use of a sling, with proper positioning of the arm at night to restore the normal anatomic alignment of the shoulder joint.

Occasionally, one may encounter multiple peripheral manifestations in the paralytic upper extremity without any relaxation of the shoulder joint. These patients present the symptom complex referred to as the shoulder-hand syndrome. Chevallier[2] in 1867 called attention to vasomotor disturbances in hemiplegic patients. Later, Sudeck[3] described post-traumatic atrophy of the hand after injury. Miller and de Takats[4] referred to it as a post-traumatic dystrophy. Evans[5] summarized 57 cases of reflex sympathetic dystrophy occurring in a number of disabilities, including a hemiplegic patient. Steinbrocker[6] clearly defined the total picture of the shoulder-hand syndrome in reflex dystrophy of the upper extremity. He included a hemiplegic patient in his series. Repeated sympathetic blocks were recommended by several authors for the treatment of this syndrome. Swan[7] described the shoulder-hand syndrome in three cases after hemiplegia. Betcher and Casten[8] outlined the criteria for the treatment of various stages of the disability as classified originally by Steinbrocker. Most recently, Rosen and Graham[9] reviewed 73 patients with shoulder-hand syndrome. They called attention to the need for early recognition of this disability. There were several patients with cerebral lesions included in their series. In the past three years, we encountered six cases of reflex sympathetic dystrophy of the upper extremity during the rehabilitation of a large number of patients with cerebral vascular lesions.

Report of Cases

Case 1.—A 67-year-old male had a cerebral thrombosis with hemiplegia on the right side and moderate degree of expressive aphasia. Five months later, he complained of severe pain in the right upper extremity involving the shoulder, elbow, and the fingers. The hand and the fingers were swollen, the skin was red and warm, and there was marked limitation of passive motion in the fingers. Conservative treatment including heat, massage, and passive exercises gave no relief. After a right stellate ganglion block, there was immediate alleviation of the pain in the hand and fingers. The swelling subsided and there was some return of voluntary function. Active exercises were instituted without pain. However, pain and limitation of motion in the shoulder persisted. The shoulder pain was relieved by a right suprascapular nerve block but motion was unchanged. The elbow was completely stiff due to the development of an extensive heterotrophic calcification (fig. 1).

Case 2.—A 60-year-old male had a cerebral thrombosis which resulted in hemiparesis on the right side with expressive aphasia. He improved to the extent that he was ambulant and able to use his right hand. One year later, he developed progressive pain in the right shoulder. The hand and fingers became stiff and swollen with increased skin temperature, and there was progressive loss in shoulder motion. All attempts at motion were strongly resisted by the patient who became rather emotionally unstable. Right stellate ganglion blocks were performed on three occasions during one week. There was definite relief of pain and increase in finger and hand motion after each block, but the shoulder was unaffected. Despite vigorous physical therapy, the symptoms in the hand recurred. High thoracic sympathectomy on the right at the level of T-2 and T-3 was performed, with prompt improvement in the symptoms. After vigorous treatment he regained a considerable degree of painless function in the hand and fingers but the shoulder remained partially frozen (fig. 2).

Case 3.—A 42-year-old female developed hemiplegia on the left side after craniotomy for excision of a meningioma. She had some function in the lower extremity, but the arm was flaccid with painless, passive complete motion. During the course of her physical rehabilitation she developed a burning pain in the left hand and fingers associated with swelling, obliteration of the interphalangeal joint creases,

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stiffness, and trophic changes in the skin. Passive motion of the hand and fingers became progressively intolerable and the patient became emotionally unstable. A left stellate ganglion block was performed with temporary amelioration of the symptoms. However, the pain recurred with increased intensity. A second stellate ganglion block was done with gradual relief of pain, permitting the resumption of physical therapy. Voluntary power returned gradually over a period of several months. Seven months after discharge, there was about 90% restoration of function in the entire upper extremity without any contractures.

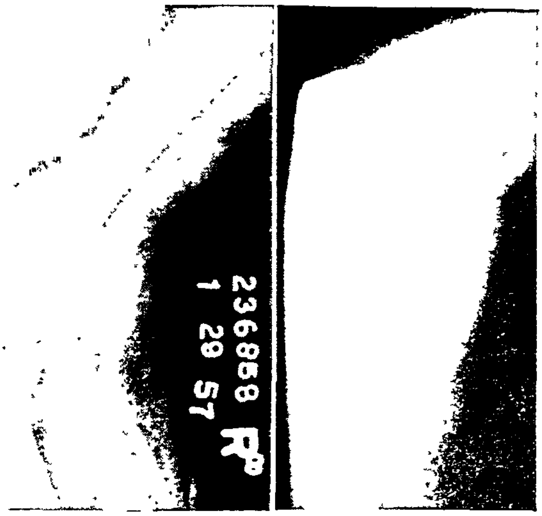

Fig. 1.—Extensive periarticular calcification of elbow in hemiplegic patient *(left)* compared with other elbow *(right)*.

Case 4.—A 70-year-old female developed hemiplegia on the left side after a cerebral thrombosis. Two months after the onset of the hemiplegia, she complained of pain in the left hand and fingers. The hand was warm, red, slightly swollen, but without pitting edema. The skin was rather smooth and glistening. All attempts at passive motion were resisted with progressive limitation of motion, particularly in the proximal interphalangeal joints. She had fairly good function in the thumb. There was prompt relief of pain after a left stellate ganglion block was done, with increased range of motion. The pain recurred within several hours with increased severity. Two subsequent blocks, with lidocaine (Xylocaine) hydrochloride, afforded temporary relief. High thoracic sympathectomy on the left at T-2 and T-3 was performed. The pain and swelling subsided gradually with some return of joint motion, permitting the resumption of active physical therapy. The interphalangeal creases reappeared. However, the contractures in the proximal interphalangeal joints remained despite the return of power in the fingers. This patient is now able to grasp and utilize the hand in an assistive capacity. Motion in the shoulder is still restricted.

Case 5.—A 48-year-old female had a cerebral thrombosis with hemiplegia on the left side. She was taught to walk with a short leg brace, but there was no return of power in the left upper extremity. Passive motion in the left shoulder became increasingly painful and restricted. Several weeks later, it was noted that the hand was discolored, slightly swollen, moist, and clammy. The fingers were flexed at the proximal interphalangeal joints but the thumb was held in extension. There was a marked degree of emotional instability. Physical therapy afforded no relief. Repeated left stellate ganglion blocks provided prompt but temporary relief. Unfortunately, this patient has refused definitive surgery.

Case 6.—A 59-year-old male with a history of coronary thrombosis had a cerebral vascular accident with hemiplegia on the left side. After two months, he complained of pain in the left shoulder, especially during the night. Subsequently, his wrist and fingers became quite painful and somewhat swollen, with marked limitation of passive motion. He had no active joint function. Two weeks of conservative therapy consisting of locally applied heat and gentle passive exercises did not relieve the symptoms. A left stellate ganglion block was performed and this brought considerable relief. Rehabilitative activities were resumed. At the present writing, there has been no return of active function in the hand, but there is practically a full range of painless passive motion with no swelling or trophic changes noted.

Comment

Although the incidence of reflex sympathetic dystrophy in hemiplegic patients is rather infrequent, early recognition and treatment is desirable in order to prevent the irreversible effects of the disability. It would be presumptuous to assume that either the sympathetic block or the sympathectomy was responsible directly for the return of active function in the hands of four of these six patients. It is more reasonable to assume that the function was inhibited by the severe pain and trophic changes, and the prompt remission of the symptoms enabled the patients to utilize the latent power in the hand.

The symptoms as presented in the six cases described have been amply discussed by previous authors, particularly Steinbrocker, and present no unusual manifestations. However, it might be interesting to note that the diagnosis of acute rheumatoid arthritis was made in case 5. All of these patients presented emotional problems such as depression and instability. The aphasic patients were presumed to have an organic brain syndrome. Observation of these cases during the course of the disability would seem to indicate that these emotional symptoms followed rather than preceded the physical manifestations in the extremity.

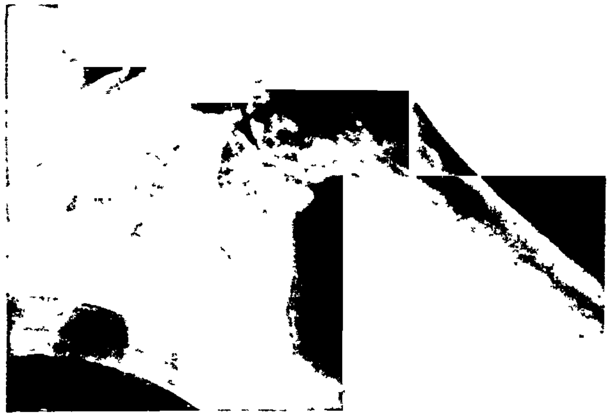

Fig. 2.—Extensive osteoporosis of frozen shoulder in hemiplegic patient.

Frequently one encounters swelling, pitting edema, and cyanosis of the hand in hemiplegic patients. This is usually due to stasis or possibly to an unrecognized thrombophlebitis. Prompt positioning of the extremity with adequate physical therapy usually relieves this condition. In patients presenting the syndrome of reflex sympathetic dystrophy, the swelling is usually less pronounced, without pitting edema but with rather marked trophic changes in the skin. The proximal interphalangeal joints are primarily involved. X-ray examination during the later stages reveals the typical changes in the carpal bones, as originally described by Sudeck, consisting of spotty demineralization which persists even after the patient has improved. Figure 3 illustrates the hands of the patient in case 1, and figure 4, by contrast, shows the x-rays of the hands of a hemiplegic patient without any dystrophic changes.

Early recognition of the disability is important since the contractures in the fingers may become irreversible in a relatively short time. Prompt blocking of the stellate ganglion with short-acting anesthetics, such as procaine or lidocaine, can be utilized as a diagnostic–therapeutic procedure. In some cases it was noted that the symptoms recurred with increased severity after the temporary relief afforded by the first stellate ganglion block. In case 4, considerable persuasion was necessary to get the patient to consent to an additional blocking procedure. Sympathectomy was performed only after repeated blocks had failed to produce a lasting remission. Symptoms referable to the shoulder, including pain and limitation of motion, were not favorably affected by either the blocks or the sympathectomy.

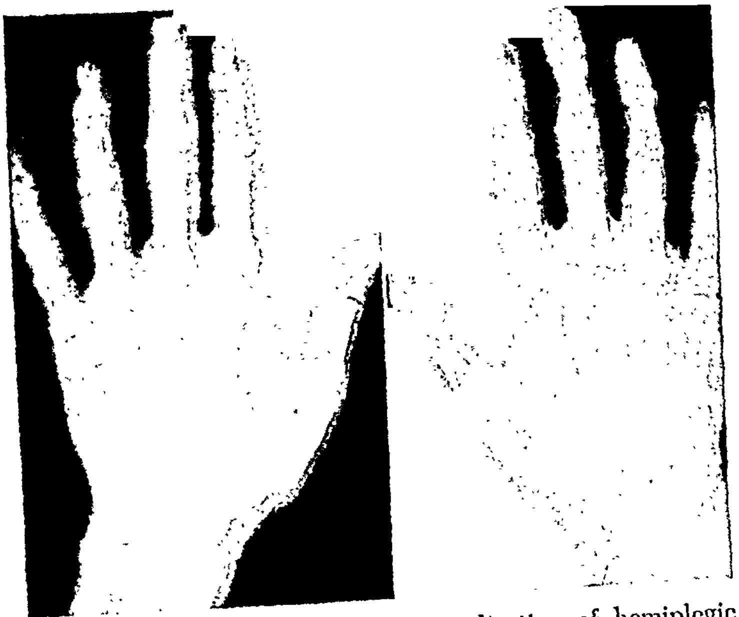

Fig. 3.—Persistent spotty demineralization of hemiplegic hand two years after treatment *(right)* compared with normal hand *(left)*.

Summary

As observed in six cases of posthemiplegic reflex sympathetic dystrophy of the upper extremity, early recognition of this unusual complication is necessary to prevent irreversible contractures and disability. Ipsilateral stellate ganglion blocks are an important diagnostic-therapeutic procedure in the early stages of this disability if they are followed by adequate mobilization. If repeated blocks have given temporary relief, high thoracic sympathectomy is the definitive treatment of choice. The underlying shoulder disability is unaffected by the blocks or sympathectomy.

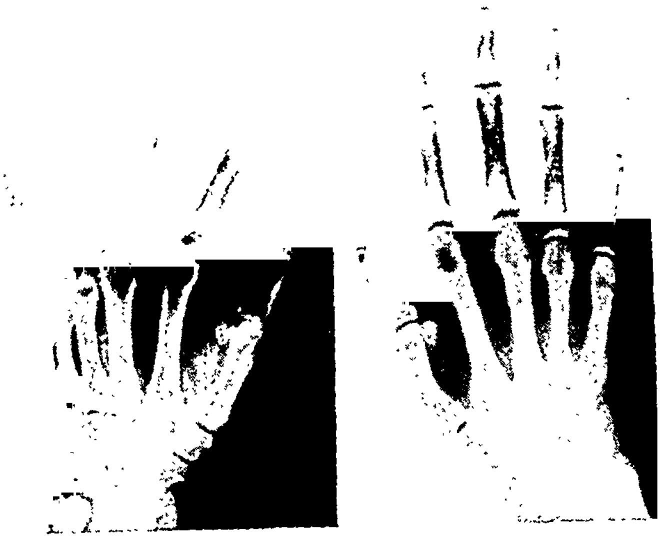

Fig. 4.—Hemiplegic hand without dystrophic change *(left)* and uninvolved hand of same patient *(right)*.

Addendum

Since the completion of this report, two additional patients have responded favorably to stellate ganglion blocks and vigorous physical therapy.

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CLINICAL NOTES

INTRA-ARTICULAR ADMINISTRATION OF HYDROCORTISONE IN HIGH CONCENTRATION

USE IN TREATMENT OF ARTHRITIC KNEES

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The value of hydrocortisone given intra-articularly in the treatment of arthritis has been well established by a number of investigators. In addition to hydrocortisone acetate, various analogues and derivatives of hydrocortisone have been studied. As a result of these studies, certain specific dose recommendations have been made.

Hollander and associates[1] have studied extensively this means of therapy and in one study based on 1,700 injections[1c] suggested that the way is open to finding analogues or esters of hydrocortisone having still more lasting palliative effect. Hollander has recommended injections of from 25 to 50 mg. of hydrocortisone acetate, with 50 mg. as the maximum dose.[1d] This upper-dose recommendation was based on the apparent inability of the synovial lining of the joint to absorb efficiently a greater quantity of the drug because of the "overflow effect" leading to systemic manifestations. In my experience, however, doses of this magnitude have not achieved optimum results. Improvement has been inadequate and too transient to be completely satisfactory either to the physician or to the patient.

Table 1.—*Response of Sixty Patients with Arthritis to Various Steroid Preparations**

	Patients		Improvement					
				Duration, Days				
	No. Injected	No. Improved	Grade†	Min.	Av.	Max.	Injections, Total No.	Patients with Systemic Effects, No.
Hydrocortisone acetate, 25-50 mg	60	45§	2-3	3	6	14	262	5
Hydrocortisone tertiary-butylacetate, 25-50 mg.	60	51	2-3	3	11	30	186	2
Hydrocortisone acetate, 150-300 mg.‡............	60	56‖	1-2	21	34	80	303	<40¶
Hydrocortisone acetate, 250 mg./cc............	40	38	1-2	20	31	76	235	36
Prednisolone acetate, 25-50 mg.	50	40	2-3	5	10	25	95	7

* Eleven patients had osteoarthritis and 49 had rheumatoid arthritis.

† Grade 4, little or no relief; grade 3, moderate relief; grade 2, marked relief; grade 1, complete relief.

‡ Some preparations contained neomycin, 5 mg. per milliliter.

§ Of the patients whose condition did not improve, six had osteoarthritis and nine had rheumatoid arthritis.

‖ Of the patients whose condition did not improve with large doses, three had osteoarthritis and one had rheumatoid arthritis. The two patients whose condition did not improve after therapy with 250 mg per cubic centimeter of hydrocortisone acetate also showed no improvement after therapy with 150 to 300 mg. of hydrocortisone acetate (column 3).

¶ Systemic effect was not evaluated in every patient.

The Present Study

The purpose of this study was twofold. First, I was interested in a comparative evaluation of the effects of various compounds of hydrocortisone when injected into the joint cavity. My second interest concerned the effect of comparatively high doses of hydrocortisone acetate by this route. In pursuit of my first objective, I evaluated hydrocortisone acetate and hydrocortisone tertiary-butylacetate. More recently I have studied the acetate of Δ^1-hydrocortisone (prednisolone acetate).

Several investigators[2] have reported the increased duration of symptomatic relief obtained after the use of hydrocortisone tertiary-butylacetate in a large proportion of patients. In a minority of patients, a greater degree of symptomatic relief was achieved than with equivalent doses of hydrocortisone acetate. However, not all patients have responded to the tertiary-butylacetate, and a significant number have been noted to achieve greater relief of symptoms and signs from the acetate than from the tertiary-butylacetate. In general, my experience with hydrocortisone tertiary-butylacetate has paralleled that of other investigators. I found it to be somewhat more effective than the acetate and to approximately double the average duration of symptomatic relief over that of hydrocortisone acetate in the majority of patients. In others, however, it proved to be inadequate.

Because of the inadequate response in some patients to doses of the order of 25 to 50 mg., I proceeded to increase the dose of hydrocortisone acetate far beyond this usual dose. It was my feeling that in large joints the greater area of synovial tissue should permit a greater absorption of hydrocortisone. The preparations used in this study were furnished in concentrations of 50, 100, 150, and 250 mg. per milliliter. Some contained neomycin, 5 mg. per milliliter, as an antibacterial agent.

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Sixty patients were studied with reference to the degree and duration of response to different preparations and to varying doses. The knee joint was used throughout the study. The group consisted of 11 patients with osteoarthritis and 49 patients with rheumatoid arthritis. The patients shown in the first column of table 1 received hydrocortisone acetate in the usually administered dose of 25 to 50 mg. Next, in column 2, are the results of tests with the higher ester, hydrocortisone tertiary-butylacetate, with the dose still held at the 25-to-50-mg. level. In the third column are recorded the results with the large doses (150-300 mg.) of hydrocortisone acetate with neomycin. Hydrocortisone acetate, 250 mg. per milliliter, was employed in the 40 patients shown in column 4. Prednisolone acetate, 25-50 mg., produced the results depicted in the last column.

TABLE 2.—*Systemic Effects in Patient with Rheumatoid Arthritis, Stage 2, Class 3*

Date, 1955	Knee Injection (Hydrocortisone Acetate), Mg.	Eosinophil Count, No./Cu. Mm.	Steroid Excretion, Mg./24 Hr.	
			Free, Porter-Silber*	Free, Gornall-McDonald†
2/19		568		
2/20		481	0.588	
2/22			0.591	
2/23		380	0.478	1.025
2/24	250‡	258 (8 a.m.)	0.745	1.59
2/25		120	1.148	2.96
2/26		0	1.739	3.08
2/27		6	1.423	2.65
2/28		0	1.358	
3/1		109	1.190	1.91
3/2		240	0.040	1.01
3/3				1.44
3/4	250‡	371 (8 a.m.)		1.41
		212 (at 6 hr.)		
		100 (at 24 hr.)		
3/5		25		2.77
3/7		40		6.84
3/8		34		4.20
3/9		80		2.70
3/10		69		1.79
3/11		200		
3/12		131		
3/13		250		
3/14		206		
3/15		212		
3/16		230		1.015
3/17		258		
3/18		303		
3/21		260	0.445	1.60
3/22				
3/23	250‡	287 (8 a.m.)	0.334	
		200 (at 5 hr.)	1.115	
		110 (at 18 hr.)	1.605	
3/24				5.77
3/25		48	1.710	8.00
3/28		60	1.402	5.65
3/29		24	1.113	3.80
3/30		68	0.890	3.77
3/31		160		
4/1		203	0.468	1.98
4/2		281		1.55
4/4		290	0.523	1.13
4/5		275		
4/6		304		

* Porter and Silber: J. Biol. Chem. 185:201, 1950. Kassenar and others: Acta endocrinol. 18:60, 1955.

† *Gornall and McDonald:* J. Biol. Chem. 201:279, 1953.

‡ Intra-articular, at 8:30 a.m.

I was particularly impressed by the results obtained with the higher dose range (150-300 mg.) of hydrocortisone acetate. Significantly, both the number of patients who obtained relief and the degree of relief obtained were greater than was observed with the same preparation in 25-to-50-mg. doses. Of equal or perhaps greater importance, the duration of improvement rose from an average of 6 days to an average of 34 days.

It is interesting to note that in column 3 there are 56 patients with conditions improved (93.3%) as compared with 45 patients (75%) in column 1. The degree of improvement, however, points up the real significance of the results. Along with an 18.3% increase in the number of patients with their condition improved by larger dosage, the marked improvement from grade 3 in column 1 to grade 1-2 in column 3 is striking.

It has been noted by other investigators[3] that hydrocortisone is systemically absorbed from the joint cavity. Clinical manifestations of this absorption were reported by Ward and Mason,[3b] who noted that in 21% of their patients a generalized antirheumatic effect followed intra-articular injection of hydrocortisone acetate. Ninety per cent of those patients in whom a systemic effect was observed received intra-articular injections of 50 mg. or more. In this group, improvement in uninjected joints was observed to follow the intra-articular injection of hydrocortisone in a single joint. Coincident with the quantitative and qualitative improvement observed with the larger dose of hydrocortisone acetate in our series was an increase in the incidence of systemic manifestations. These rose from 5 (column 1) to over 40 (column 3). Subjective improvement in other affected but uninjected joints was the clinical manifestation noted. A reduction in total eosinophil count and an increase in the amount of 17-hydroxycorticosteroids in the urine was also noted. Table 2 contains data on eosinophil count and steroid excretion that are illustrative of the systemic effect produced. The occurrence of systemic effects was coincidental and not intentional. However, these effects caused no difficulty and, in fact, seemed to evoke gratitude from many patients. There were no "flare ups" after systemic relief disappeared. The neomycin included in some of the preparations produced no evidence of reaction in the joints and no evidence of systemic toxicity. Urine examination revealed no change after the administration of neomycin.

Summary and Conclusions

Larger doses of hydrocortisone acetate than heretofore generally employed may be injected into the larger joints such as the knee joint, with quantitative and qualitative improvement in results over those obtained with smaller doses. Quantities of hydrocortisone acetate suspension as great as 5 to 6 cc. were given without reaction either to the volume or to the amount of hydrocortisone.

No toxic or other untoward effects were noted with the injection of neomycin in amounts up to 25 to 30 mg. into the joint. The addition of neomycin affords effective antibacterial protection against possible septic infection of the joint. Systemic effects manifested by improvement of uninjected joints, lowered eosinophil counts, and increased urinary steroid values occurred with larger doses of hydrocortisone acetate.

These findings suggest that the larger joints, such as the knee, have a greater capacity than heretofore believed to hold a larger quantity of hydrocortisone in the cells. Thus a greater and more intense degree of improvement as well as an increased duration of relief will follow.

Addendum

Since this paper was prepared for publication, similar clinical and laboratory results have been reported in five patients by Fujita.[4]

40 North St. (2).

The hydrocortisone tertiary-butylacetate, 25 mg. per ml., used in this study, was supplied by Merck, Sharp & Dohme, Rahway, N. J. The prednisolone acetate, hydrocortisone acetate (50 mg. per milliliter with neomycin, 5 mg. per milliliter), and other hydrocortisone acetate preparations in concentrations of 50 mg. to 250 mg. per milliliter were supplied by the Upjohn Company, Kalamazoo, Mich.

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CHERNEY INCISION IN UROLOGIC SURGERY

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The urologist has occasion to utilize surgical procedures which necessitate an easy access to the deepest pelvic recesses. An adequate incision will facilitate these deep pelvic operations and result in reduced surgical trauma to the patient and lessened strain on the surgeon. The Cherney incision, with division of the tendinous insertions of the rectus muscles at the symphysis and with lateral extension, gives pelvic access superior to that of any previously described incision.

Pfannenstiel, in 1900, suggested transverse division of the lower abdominal skin and fascia with separation of the rectus muscles. In 1907, Maylard and Bardenheuer modified the Pfannenstiel incision by dividing all the lower abdominal layers transversely. Maylard, in a paper supplemented by excellent drawings, discussed the transverse incision for abdominal walls in obese patients. He stressed its many advantages during and after operation on the upper abdomen, including the lessened likelihood of a postoperative hernia. In 1941, Cherney reported his modified transverse incision with separation of the rectus muscles from the symphysis. In 1946, Smith stated that the Cherney incision was readily adaptable to surgery of the bladder, diverticula, and lower ureters. Culp and DeWeerd, in 1953, discussed the advantages of the Cherney incision and stated that the "incision has inherent advantage which cannot be equalled by any other type of incision and . . . difficult pelvic urologic operations which so frequently confront the urologist can be performed with less wear and tear on both the patient and the surgeon if the Cherney incision is used."

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In 1955, Cherney reported on 808 surgical cases following detachment of the recti from the symphysis and pelvic bones. There were six (0.75%) wound disruptions and five (0.6%) postoperative hernias. He again pointed out the technical simplicity, adequate exposure, healing resulting in a strong abdominal wall, postoperative comfort, and cosmetically pleasing scar.

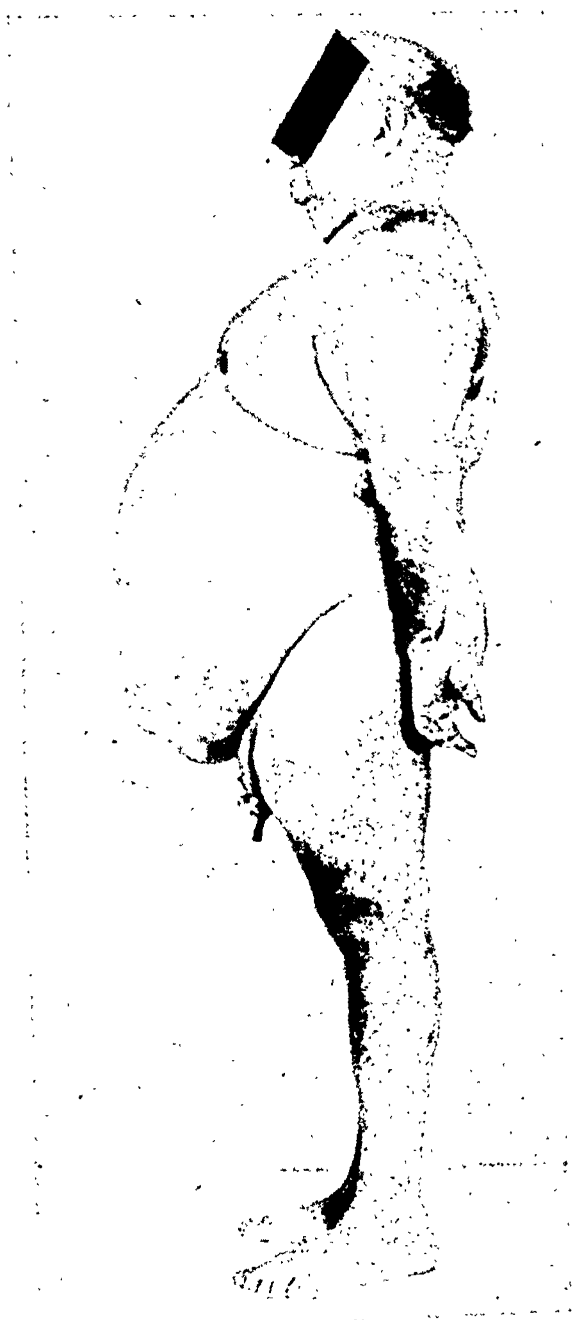

Fig. 1 (case 1).—Preoperative photograph showing large pendulous abdominal wall and large umbilical hernia (1955).

We first used a modified Cherney incision in 1945. In patients requiring a total cystectomy the tendinous rectus insertions were divided about 1 cm. above their insertion. There was difficulty in closing the modified incision, and the procedure was abandoned. Soon after Cherney's article appeared in January, 1955, a patient appeared in whom the Cherney incision seemed strongly indicated. The use of the Cherney incision simplified what would probably have proved a hazardous suprapubic prostatectomy with a complicating umbilical hernia.

Report of Cases

Case 1.—A man, aged 70, was admitted to Passavant Memorial Hospital on Feb. 12, 1951, with a history of gross hematuria four days before. Examination revealed an obese individual weighing 300 lb. (181.4 kg.) (fig. 1). The general physical examination was noncontributory except for discovery of a large umbilical hernia and an enlarged prostate, grade 2+. The blood pressure was 152/86 mm. Hg. The urine now was clear with an occasional red blood cell and white blood cell. A tumor of the bladder was suspected. We were unable to pass a cystoscope or a resectoscope. A cystogram revealed a filling defect on the bladder floor, possibly a middle prostatic lobe or neoplasm (fig. 2). The anterior urethral strictures responded to an indwelling catheter. The patient was readmitted to the medical service five times during the next four years for a weight reduction program. He was a connoisseur of foods and cooking and rapidly regained weight after each discharge from the hospital.

On Jan. 11, 1955, he was readmitted for gross hematuria and acute urinary retention. A futile effort was made to pass a long resectoscope through the site of a perineal urethrotomy. A suprapubic operation became mandatory. Because of the patient's large umbilical hernia, two of us performed the suprapubic prostatectomy. The Cherney incision was selected to avoid rectus muscle separation and encroachment upon the umbilical hernia. The pendulous abdominal wall was supported by two assistants during the operation. The Cherney incision proved ideal and allowed easy access to the bladder and enlarged prostate. A benign adenoma weighing 122 Gm. was removed. An indwelling catheter and drains were put in place, and the incision was closed by suturing the tendinous ends of the rectus muscles to the under surface of the fascia with fine interrupted silk sutures.

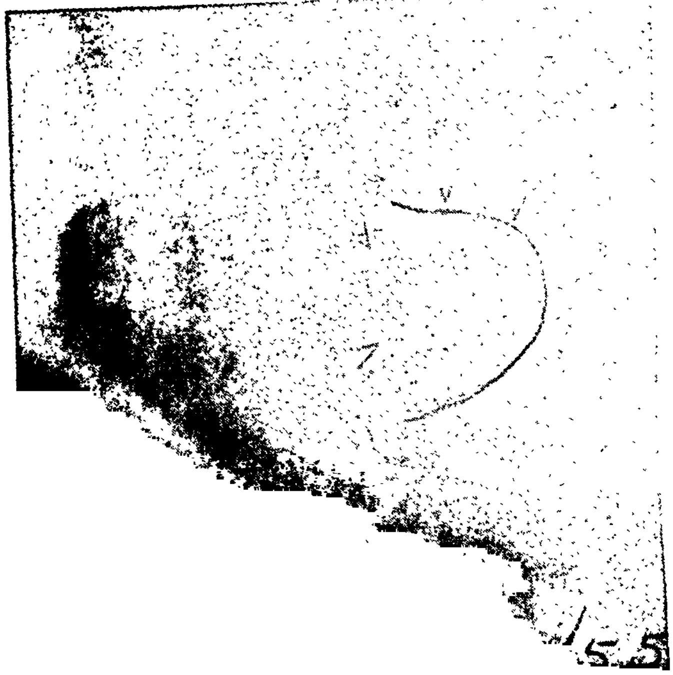

Fig. 2 (case 1).—Cystogram showing large tumor on floor of bladder encroaching on bladder outlet.

The abdominal fascia and skin were then likewise closed with interrupted silk sutures. The convalescence was uneventful, the wound healed well, and the abdominal wall appeared strong. A checkup in June, 1957, revealed mild anterior urethral coarctations. The patient was still obese, asymptomatic, and enjoying retirement in a Florida atmosphere. The scar from the transverse incision was inconspicuous, the wound was well healed, and the wall was strong (fig. 3). The large abdominal hernia, now 24 cm. in diameter, remains asymptomatic.

There are many other pelvic urologic operations where maximum exposure is mandatory in order to reduce morbidity and facilitate the procedure; these include cystectomies, segmental bladder resections, reimplantation of ureters into the bladder, bladder fistula, bladder diverticula, seminal vesiculectomies, and radical prostatectomies. The Cherney incision has been used to marked advantage and with no untoward complications in conjunction with four recent radical retropubic prostatectomies. In case 2 is reported a radical retropubic prostatectomy for early carcinoma complicated by a symptomatic inguinal hernia on the left side. The hernia was repaired intrapelvically before the Cherney incision was closed.

Case 2.—A man, aged 69, admitted Jan. 13, 1957, complained of difficulty in voiding, small urinary stream, diuria, nocturia, and pain at the base of the penis. The general physical examination was noncontributory except for discovery of the grade 1 nodular prostatic enlargement and a symptomatic left inguinal hernia. The patient had had hernial repair on the right side in 1947 and a cholecystectomy in 1949. The medical survey revealed no contraindication to surgery. Intravenous pyelography revealed an intravesical prostatic enlargement, a renal cyst on the left, and no evidence of bone metastasis (fig. 4). The acid phosphatase level was 3.26 King-Armstrong units per 100 cc. The blood urea nitrogen level was 17.6 mg. per 100 cc., blood sugar level 77 mg. per 100 cc., and the blood cell count and differential normal. A transurethral biopsy and vasectomy were carried out. The microscopic sections showed adenocarcinoma of the prostate. It was thought that this patient's carcinoma was sufficiently confined to allow a radical prostatoseminal vesiculectomy.

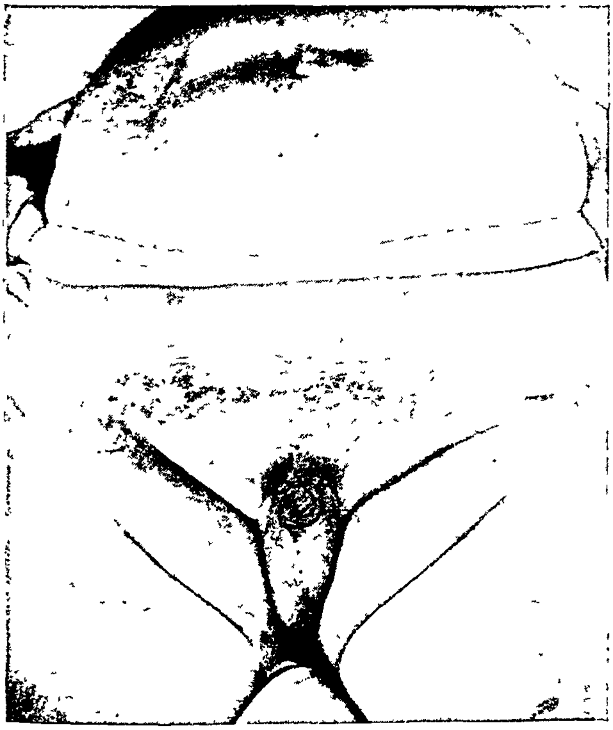

Fig. 3 (case 1).—Postoperative inconspicuous but strong transverse Cherney incisional scar and large umbilical hernia (1957).

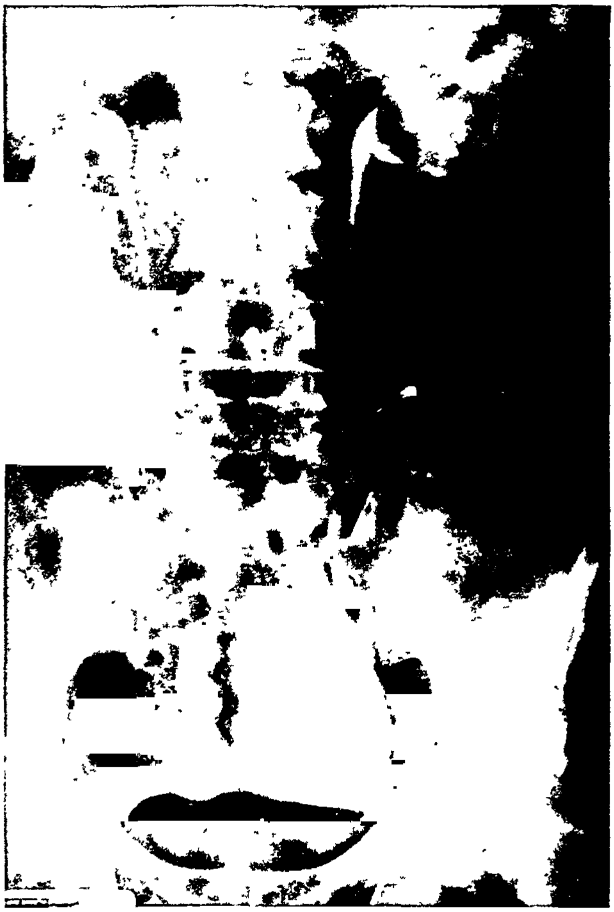

Fig. 4 (case 2).—Excretory pyelogram showing intravesical prostatic enlargement, asymptomatic left pyelographic defect suggesting cyst, and normal pelvis and lumbar spine.

On Jan. 28, 1957, the removal of the prostate and seminal vesicles was easily carried out by the retropubic approach through the Cherney incision. After the anastomosis of the bladder to the urethra, intrapelvic hernial repair was done by suturing the transversalis fascia to the adjacent periostium of the left pubic bone. The tendinous rectus insertions were resutured to the symphysis, and the remaining wound was closed with fine interrupted silk sutures. The patient made an uneventful recovery except for a perivesical abscess which developed on the right side three weeks after the operation. The infection necessitated surgical drainage. This increased his hospital morbidity. He was discharged on the 40th postoperative day with mild stress and strain incontinence. A follow-up study showed improvement in incontinence and no demonstrable evidence of residual carcinoma.

A fear still exists among urologic surgeons that division of the rectus insertions entails undue risk and postoperative wound disruption. When these wounds are healed, they are asymptomatic and the walls are strong. When the insertions are attached to the abdominal wall fascia, as is possible with this incision, the sutures may be placed without undue tension. The pelvic exposure accomplished through the Cherney incision is unequalled by any other type of low abdominal incision. The incision allows comfortable access to the remote pelvic recesses in very obese patients. When indicated, intrapelvic hernial repair is feasible with the Cherney incision without increasing the operative morbidity.

Summary and Conclusions

The Cherney incision is extremely useful in urology for pelvic operations on the bladder, prostate, seminal vesicles, and urethra. In obese patients, it is the incision of choice for pelvic urologic operations. Wound healing is strong and is followed only occasionally by disruption and hernia.

720 N. Michigan Ave. (Dr. Riba).

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MEDIAN NEURITIS (CARPAL TUNNEL SYNDROME) CAUSED BY GOUTY TOPHI

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The syndrome resulting from compression of the median nerve at the wrist has been designated variously: median neuritis, median thenar neuritis, professional or occupational median neuritis, thenar neural atrophy, partial thenar atrophy, thenar palsy, tardy median palsy, median neuropathy, and, most commonly at present, carpal tunnel syndrome.

Recognition of this syndrome has evolved slowly. get[1] a century ago called attention to the late evelopment of disturbed function of the median nerve after fractures of the wrist; this delayed, or tardy, median palsy was ascribed by him to compression of the nerve under the transverse (or volar) carpal ligament by the presence of callus or of thickened and indurated tissues adjacent to the nerve. In 1909, Hunt suggested that thenar atrophy might be caused by compression of the thenar branch of the median nerve as it emerged from beneath the transverse carpal ligament; later he attributed the lesion to compression of the median nerve beneath the ligament.[2] Marie and Foix[3] in 1913 and Moersch[4] in 1938 noted that the median nerve might be compressed beneath the transverse carpal ligament and suggested the possibility of treatment by section of that ligament. Woltman[5] in 1941 and, subsequently, Zachary,[6] Cannon and Love,[7] and Brain and associates[8] reported the successful treatment of median neuritis by means of surgical decompression of the nerve. Since then recognition of the condition has become more widespread and reports of its successful surgical treatment have been numerous.

As the syndrome has become known more generally, so too have increased the suggested causes of compression of the median nerve in the carpal tunnel: the late effects of major trauma,[1] occupational microtrauma,[2] acromegaly,[5] osteoarthritis,[9] nonspecific thickening of the transverse carpal ligament[10] or flexor tendon sheaths,[11] rheumatoid arthritis,[10] amyloid disease,[12] myxedema,[13] neuroma,[7] Léri's pleonosteosis,[14] anomalous artery,[9] impingement by a slip of the sublimis muscle,[9] carpal ganglion,[15] and idiopathic nocturnal swelling of the hands.[16] Rheumatoid arthritis with tenosynovial swelling about the flexor tendons at the wrist is one of the commoner causes of the carpal tunnel syndrome in our recent experience.

We have encountered a case of bilateral compression of the median nerve at the wrist with resulting neuritis, unique in that compression was caused by the presence of large urate deposits in and about the carpal tunnels.

Report of a Case

A 56-year-old man, seen at the Mayo Clinic in January, 1957, complained of pain, weakness, and numbness of the fingers of both hands during the preceding two years. In 1942, he had had his first attack of acute gouty arthritis, and shortly thereafter hyperuricemia was discovered. From 1942 to 1948 he had four more attacks of moderately severe acute gouty arthritis. In 1948, an unusually severe and prolonged attack involved the ankles and several joints of the feet. Subsequently, the ankles and feet had remained

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chronically swollen and painful; frequent attacks of acute gouty arthritis involved one or more joints, especially the metatarsophalangeal and tarsal joints, ankles, knees, wrists, elbows, and finger joints. Since 1950, tophaceous deposits had enlarged gradually on the flexor aspects of both wrists, on the ears, about the first metatarsophalangeal and various finger joints, in the olecranon bursae, and at the insertion of the Achilles tendon. In 1953 and again in 1954 large tophi had been excised from the region of the first metatarsophalangeal joints, left ankle, and both olecranon bursae. Both times the procedure had been followed by severe attacks of acute gouty arthritis. Prior to 1953 the patient had not followed prescribed treatment for gout, but since then he had been taking 0.5 Gm. of probenecid (Benemid) and 1/100 grain (0.6 mg.) of colchicine once or twice daily.

About two years preceding his visit to the clinic in 1957 the patient began to note intermittent numbness and tingling of the first four fingers of both hands and pain in those fingers and in the wrists, particularly when he used his wrists and fingers. The fingers, especially the thumbs, gradually weakened. Numbness and pain of the fingers and pain at the wrists worsened. He became almost incapacitated in respect to use of the hands.

The patient was moderately obese, and on physical examination numerous tophi of various sizes were seen on the ears and about the proximal interphalangeal and metacarpophalangeal joints, wrists, olecranon bursae, ankles, metatarsophalangeal joints, and the insertion of the Achilles tendons. The tophi on the flexor aspects of both wrists were 3-4 cm. in diameter. Muscles of the right thenar region were atrophic. Thenar, hypothenar, and interosseous muscles of both hands were slightly weak, those of the right hand being weaker than those of the left hand. There was hypesthesia in the distribution of the median nerve in the right hand.

Results of laboratory examinations were normal except as follows: concentration of uric acid was 10.2 mg. per 100 cc. of serum and roentgenograms of the wrists and hands showed evidence of osteoporosis, more marked on the right than on the left.

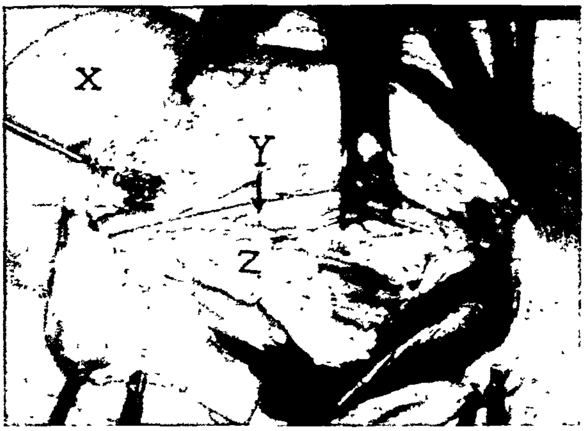
Electromyographic examination with a needle electrode did not reveal evidence of fibrillation or fasciculation in the right opponens pollicis and abductor pollicis brevis muscles. Voluntary contraction of these muscles evoked motor-unit potentials of normal size, but the number of these potentials from the right opponens and abductor pollicis brevis muscles was slightly reduced. Electric stimulation of the median nerves with a maximal stimulus for motor fibers yielded the following results: The amplitude of the action potential of the thenar muscles was just below the normal range in both hands; the latency of the response or "conduction time" between the moment of stimulation of the median nerve just proximal to the carpal tunnel and the beginning of the action potential of the thenar muscles was prolonged bilaterally, being 6.1 msec. on the right and 6.9 msec. on the left. The upper limit of normal is 5 msec. Conduction velocities of the median nerves from the elbow to the wrist proximal to the carpal tunnel were within the normal range.

Our diagnosis was bilateral median neuritis, or carpal tunnel syndrome, owing to compression of the median nerves by tophaceous deposits. On Jan. 17, 1957, the median nerves were decompressed by means of excision of tophi from the wrists and section of the transverse carpal ligaments (see figure). Bilaterally, there were a few tophi in the superficial tendons and extensive tophaceous deposits in the deep flexor tendons and tendon sheaths, with considerable fibrosis surrounding the tophi. A large mass of urate crystals, about the size of a golf ball, was located beneath the deep flexor tendons and above the interosseous membrane and pronator muscles bilaterally. The right transverse carpal ligament was greatly thickened by multiple tophaceous deposits, and the median nerves of both hands obviously were compressed by tophaceous masses. The pathologist found the excised masses to be composed of urate crystals.

After operation, a severe flare of acute gouty arthritis involved several peripheral joints; treatment with 25 grains (1.6 Gm.) of aspirin three times daily by mouth, colchicine, and dextrose administered intravenously was successful. After operation, the patient experienced a temporary slight increase in sensory loss and muscle weakness in the median distribution of the right hand; the left hand was normal in strength and sensation, although occasional paresthesias persisted. He was dismisssed on Jan. 30, 1957, at which time the operative wounds were healed. He was advised to follow a diet low in purine, to reduce his weight, and to take 2 Gm. of probenecid daily and 2 Gm. of sodium bicarbonate three times daily. Four months later he reported marked improvement in strength and sensation in his hands and was able to play golf for the first time in 18 months.

Comment

To the growing list of conditions recognized as causes of compression of the median nerve beneath the transverse carpal ligament, this case adds another, namely, gouty tophaceous deposits. Although tophi are seen more commonly in certain other locations, they do occur occasionally at the wrist. Undoubtedly other instances of the carpal tunnel syndrome caused by gouty tophi will be found if sought.



Findings at operation on right wrist: X, base of thumb; Y, median nerve; and Z, tophaceous mass. Transverse carpal ligament has been sectioned.

Proper treatment for gout with uricosuric agents and a diet low in purine may reduce the size of tophi, but the process often is prolonged and much fibrosis and tissue thickening may remain. Thus, to afford quicker and more certain relief of symptoms and to avoid possible permanent damage, surgical decompression of the nerve would seem advisable in instances such as the one here reported.

The following manifestations of compression of the median nerve at the wrist are characteristic when the syndrome is present in its overt form: pain, paresthesias and sensory deficit in the distribution of the median nerve in the hand, and weakness and atrophy in muscles of the hand supplied by the median nerve, that is, the abductor pollicis brevis, the opponens pollicis, the superficial head of the flexor brevis pollicis, and the two lateral lumbricales. Loss of power of palmar abduction of the thumb may be more marked than weakness of opposition, since the adductor pollicis and part of the flexor pollicis brevis, which also aid opposition, are innervated by the ulnar nerve. Often the involvement of the nerve may be incomplete, thereby giving rise only to parts of the syndrome, particularly in early stages of development or in mild cases. For example, in the patient whose case is reported here the involvement on the left, although productive of distressing pain and paresthesias, was not accompanied by clinically apparent muscular atrophy or objective sensory loss. Likewise, anomalous and overlapping innervation may lead to certain variations. In a few instances, pain, apparently arising from compression of the median nerve at the wrist, has been noted to extend up the arm to levels as high as the shoulder.[17] Obviously, a careful neurological examination is required to distinguish median neuritis from protruded cervical disk, hypertrophic cervical arthritis, lesions of the brachial plexus, thoracic outlet syndrome, and generalized polyneuritis.

The following confirmatory signs of median neuritis aid in making the diagnosis: Tinel's sign, that is, tingling in the median distribution produced by tapping over the median nerve at the wrist; increased pain in the median distribution as a result of acute flexion or extension of the wrist or temporary ischemia of the extremity; and palpation of a tender swollen median nerve just above the transverse carpal ligament. We have found electromyography and measurement of the conduction time in the peripheral portion of the median nerve to be of particular diagnostic help; the characteristic findings are those of prolonged conduction time from the wrist to the thenar muscles and evidence of denervation in the muscles of the hand supplied by the median nerve.[18] As this case illustrates, prolonged conduction time may be present when signs of denervation are minimal or absent.

Summary and Conclusions

In a unique instance of bilateral median neuritis (carpal tunnel syndrome) caused by compression from gouty tophi, treatment by surgical excision of the tophi and sectioning of the transverse carpal ligaments was successful. Surgical intervention affords quicker and more certain relief than might be expected from treatment with uricosuric agents and seems to be the treatment of choice in a case of this sort. Electromyography, including measurement of the conduction time from wrist to thenar muscles in the median nerves, is an especially helpful diagnostic aid in instances of the carpal tunnel syndrome. The carpal tunnel syndrome is particularly likely to occur in patients who have some arthritic or rheumatic affliction at the wrist, such as rheumatoid arthritis, idiopathic tenosynovitis, osteoarthritis (*especially* post-traumatic), and, as illustrated, gouty tophi.

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Electromyographic examination and electric stimulation of the nerves were performed by Dr. E. H. Lambert.

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REGIONAL BLOCK AT THE WRIST OF THE GREAT NERVES OF THE HAND

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"Local anesthesia" is a term often mistakenly used to include all methods of anesthetization not included under general, topical, or spinal. There are two still-popular traditional techniques by which local anesthetics are administered: 1. The rapid insertion of the needle followed by a swift injection of all the solution that the tissues can take (fig. 1, *A*). This is used for the performance of elective procedures on the body. Quite often, one seeks for paresthesias in the nerves prior to injection. 2. The second popular method, based on equally fallacious reasoning, is used for the repair of open wounds. After the patient has suffered cleansing of the wound with tincture of green soap or one of the modern germicidal soaps (both of which cause pain), the wound is infiltrated by multiple insertions of the needle both in the proximal and distal wound edges (fig. 1, *B*).

There are several fallacies in these techniques. First, the hydrodynamic pressure of great quantities of fluid is not required to arrest nerve fiber conduction. Only enough solution is needed to bathe the nerve. Second, rapid insertion of a needle is needed to minimize pain only when the needle is large. The proper use of a tiny, no. 25 needle results in no pain when it is inserted slowly. Third, rapid pumping up of the tissues is painful. A slow injection of small amounts of solution causes no pain. Fourth, it is technically safer to inject through prepared intact skin away from the wound than through the raw tissues in the wound site. Fifth, cleansing of a wound with solutions that cause severe pain also causes concomittant severe tissue damage in addition to the original trauma. Cleansing a wound with anything prior to anesthetization causes pain and is therefore cruel. It is painless and far more humane to inject just once proximal to the wound than to inject many times into the tissues.

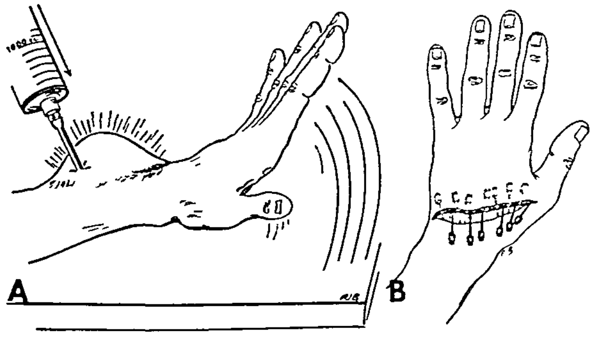

Fig. 1.—Traditional techniques for injection of local anesthetic for *A*, elective surgery, and *B*, surgery of injury due to trauma.

Regional Block Anesthesia

A more proper use of local anesthetic solutions, from bacteriological, surgical, pharmacological, and humane viewpoints, could be summarized as follows: (1) complete anesthesia for more than the site of surgery, to ensure that no part of the operative procedure shall cause pain in unanesthetized tissue; (2) painless injection; (3) bacteriologically safe site of injection; (4) use of minimal amount of solution to avoid compression of vascular and lymphatic tissue; and (5) avoidance of injection into nerves.

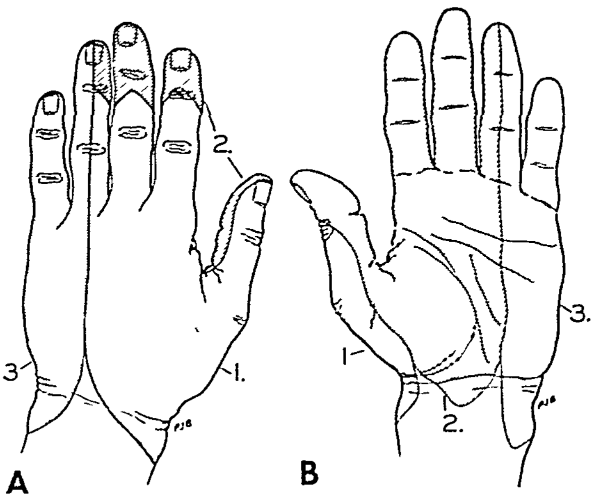

Fig. 2.—Distribution of sensory nerves in the hand. *A*, usual dorsal distribution, and *B*, usual volar distribution.

When only one digit need be anesthetized, the digital nerves are blocked in the palm and beneath the dorsal skin.[1] When more than one digit is to be anesthetized and the surgical procedure does not require the use of a tourniquet, I have found it most convenient for patient and surgeon to establish a regional block of the proper nerves to the hand at the wrist.

The proper use of a tourniquet in surgery of the hand indicates its placement high up on the upper arm. The traditional use of a rubber band or a piece of rubber tubing clamped with a hemostat as a tourniquet at the base of the finger is not only unnecessary but dangerous. If bleeding is arterial in a minor laceration, it may be stopped with pressure of a sterile sponge. If it commences again during soap and water cleansing, it will usually be of

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less magnitude and, in my experience, may be left untouched until cleansing is complete when digital pressure at the sides of the finger will arrest its flow so that the artery may be carefully clamped in a relatively sterile field under unimpeded vision.

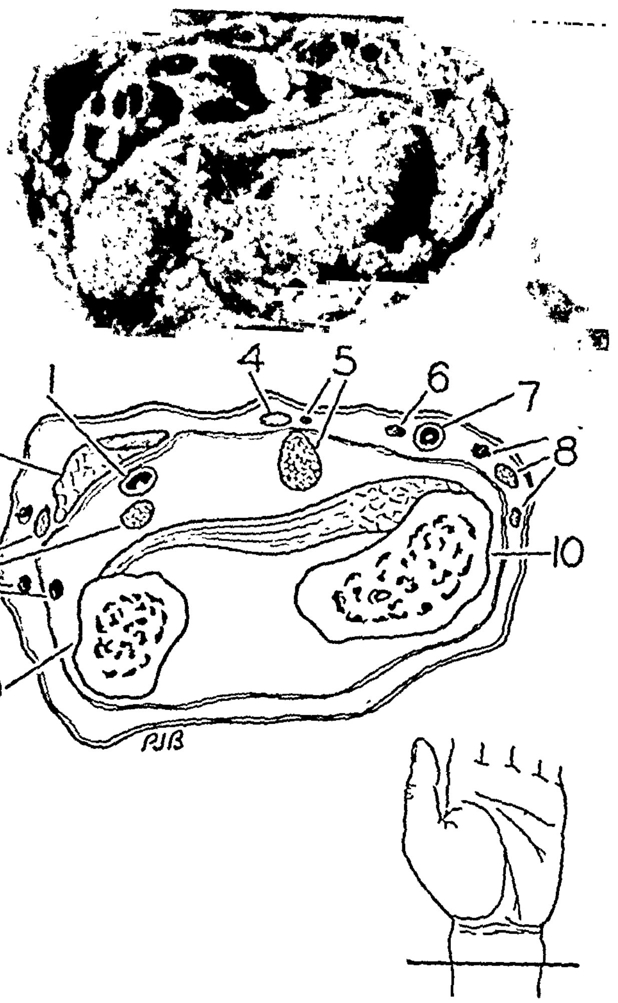

Fig. 3.—*Top*, cross-section of wrist just proximal to styloid esses of ulna and radius. *Bottom*, diagram of cross-tion: (*1*) ulnar artery, (*2*) flexor carpi ulnaris, (*3*) ulnar nerve and its branches, (*4*) palmaris longus tendon, (*5*) median nerve and its branch (variable), (*6*) anterior branch of lateral cutaneous nerve of forearm (variable), (*7*) radial artery, (*8*) branches of radial nerve, (*9*) ulna, (*10*) radius.

If trauma is extensive and bleeding profuse, direct pressure should be applied and the reparative procedure carried out in the operating room with a tourniquet high on the upper arm and a higher block[1A] or a general anesthetic.

The indications for regional block at the wrist are lacerations of the skin, skin grafts, and fractures. The contraindications may be summed up under the general heading of those conditions the treatment of which require a bloodless field with a tourniquet on the upper arm, such as injuries to tendons and nerves and severe crushing injuries.

Anatomy

In figure 2 is outlined the sensory distribution of the three nerves to the hand. Their boundaries must not be considered to be so sharply circumscribed as indicated because there is much variation in dorsal sensory nerve distribution and some overlapping of volar nerve distribution.[2] Therefore, it is discrete for the surgeon to plan to anesthetize not only the projected field of surgery but also a goodly margin about it. Another reason, too, for establishing a broad area of anesthesia is that occasionally the surgical procedure covers a larger field than anticipated.

Figure 3 shows a cross-section of the wrist just proximal to the styloid processes of the radius and ulna. There are several anatomic points to be noted here in order to simplify the anesthetization of these nerves.

First, the three nerves are no longer single nerves but have already ramified. The median nerve has sent off a variable tiny slip to the subcutaneous tissues. The ulnar nerve has divided beneath the volar fascia of the wrist and has also sent off some subcutaneous branches. The radial nerve is entirely superficial to the fascia.

Second, each nerve and its branches are either just within a relatively large fascial enclosed compartment or just superficial to a layer of fascia (subcutaneous). This fact makes for easy and sure anesthetization of each nerve without the need for eliciting paresthesias and without pumping the spaces full with ounces of anesthetic solution. This, plus the easily identified landmarks as shown be-

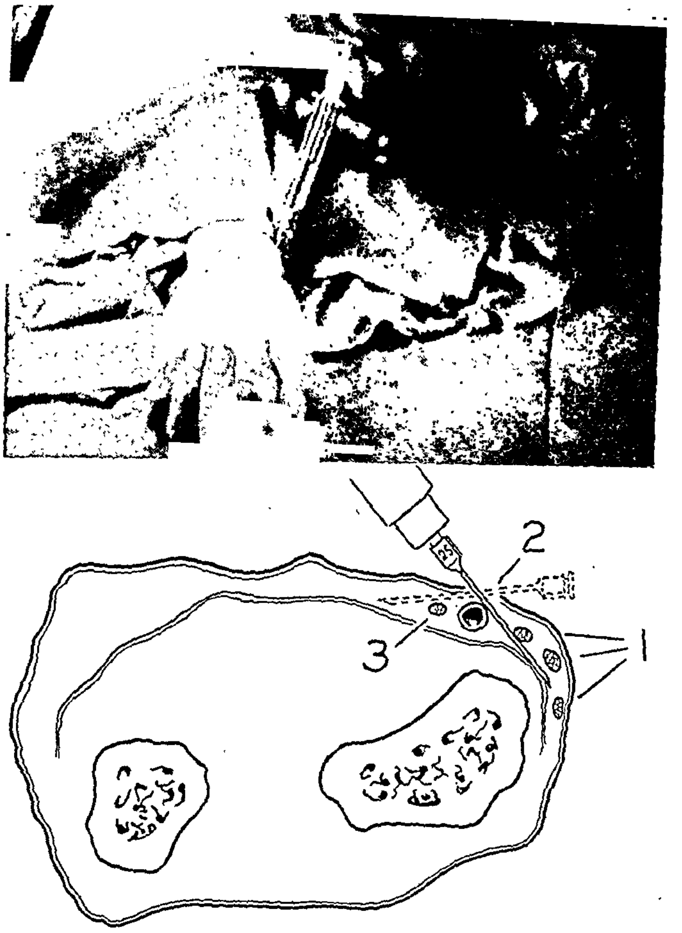

Fig. 4.—Anesthetization of radial nerve at wrist for elective procedure on thumb: (*1*) branches of radial nerve, (*2*) radial artery, (*3*) anterior branch of lateral cutaneous nerve.

low, promotes the successful bathing of each nerve with anesthetic solution, which is followed by complete arrest of nerve impulses.

Technique

I have used 2% solution of lidocaine (Xylocaine) hydrochloride with a 1:200,000 concentration of epinephrine in the uniformly successful initiation of anesthesia for 38 blocks of one or more nerves at the wrist in the past year. A 2-ml. syringe suffices for the block of one nerve or a 5-ml. syringe for the blocking of two nerves. A ⅝-in. no. 25 needle is used for all blocks. No wheals are made. If paresthesias are felt by the patient, the site of the needle point is changed.

There is never any sign of the solution having been injected until several minutes after, when an occasional surface lymphatic may have picked up some lidocaine and epinephrine; this is manifested by the appearance of some white lines in the skin of the forearm. A 10-minute wait results in complete anesthesia. The anesthesia lasts for at least two hours. Any procedure on the hand that requires more than one hour is probably of such magnitude as to require a tourniquet and, consequently, a higher block.

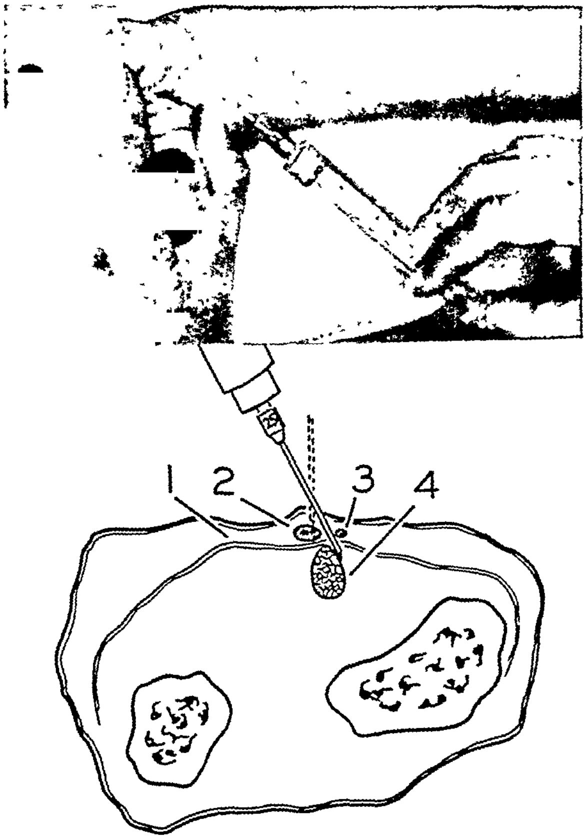

Fig. 5.—Anesthetization of median nerve at wrist for fingertip injuries (lesions are usually kept covered until anesthesia is complete; they are then cleansed): (*1*) volar antebrachial fascia, (*2*) palmaris longus tendon, (*3*) superficial branch of median nerve, (*4*) median nerve.

Radial Nerve Block.—To produce a radial nerve block, the radial artery is first palpated (fig. 4). The point of the needle is gently placed just into the skin directly over the artery, where an imperceptible amount of solution is deposited. After a hesitation of a few seconds, the needle is pressed through the skin into the subcutaneous fatty tissue, where a few minims of solution are deposited. The needle is then angled dorsally nearly parallel to the skin and is pushed through the fat to its entire length. Here the plunger is withdrawn slightly to test whether the needle is in a vein. If it is not in a vein, 1 ml. of solution is injected. Another 0.5 ml. is injected as the needle is withdrawn to its initial position, with its point just over the artery, when it is angled volarward. Again it is pressed in to its entire length and the remaining 0.5 ml. is deposited as it is withdrawn.

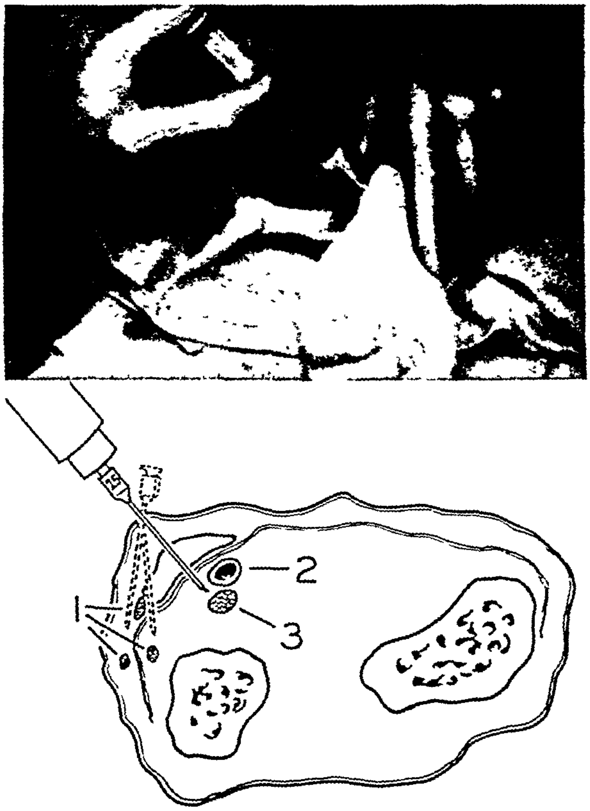

Fig. 6.—Anesthetization of ulnar nerve for elective procedure on distal palm: (*1*) branches of ulnar nerve, (*2*) ulnar artery, (*3*) ulnar nerve.

Median Nerve Block.—Note in figure 5 that there is a tiny superficial slip of the median nerve lying in the fat to the radial side of the palmaris longus tendon. The main part of the nerve lies beneath the volar fascia, either beneath or just to the radial side of the palmaris longus tendon. The top picture in figure 5 shows how the patient flexes his wrist against counterpressure with his fingers and thumb straight. This maneuver brings his palmaris longus and flexor carpi radialis tendons into sharp relief. If the wrist is fat, the tendons can be easily palpated. The needle is gently inserted into the skin and then into the subcutaneous fat (as was done for the radial nerve) directly over the palmaris longus tendon.

When the subcutaneous injection has been made, the needle is drawn to the radial side of the tendon, moving the loose skin with it. Here the needle is pressed deeper until it strikes the firm resistance of the volar fascia, where 0.5 ml. of solution is deposited. After a brief hesitation, firm gentle pressure pushes it through this layer with a definite sensation that is easily felt. The entire bevel of the point must go through the fascia, but the needle must not be pushed deeper for fear of impaling the nerve. Here, the remaining 1.5 ml. of solution is deposited and the needle removed.

Ulnar Nerve Block.—To produce an ulnar nerve block the ulnar artery is first palpated. The needle is pressed on through the skin, as above, just lateral to the artery. After the subcutaneous injection of a few minims of solution, the needle is pushed in a medial direction (fig. 6, diagram) to pass lateral to the ulnar artery. When the point has been felt to traverse the volar fascia, it is pressed on about another ¼ in., where 1 ml. of solution is deposited.

The needle is then withdrawn until the point is in the subcutaneous fat, when it is angled more dorsally and again pushed through the fascia. Another 0.5 ml. of solution is deposited in the event that there is a small branch from the main part of the nerve. The needle is again withdrawn until its point is in the subcutaneous fat, where it is angled dorsally so as to remain in the fat. It is pushed in to its full length, and the remaining solution is deposited along its tract as it is withdrawn.

Summary

The technique of regional block anesthesia of the nerves at the wrist has been employed in 38 consecutive successful blocks of one or more of these nerves in the past year. Each site of injection is easy to identify. The nerves to be anesthetized at each site are within fascial sheaths or are subcutaneous, which assures bathing the nerve with anesthetic solution without the necessity of eliciting traumatizing paresthesias.

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SPECIAL ARTICLE

DOCTOR'S MANUAL OF SPEECH DISORDERS

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Because the family physician, or the pediatrician, is almost always the first one to be contacted by the parents of a child with a speech problem, real or imagined, it is essential that the doctor know what constitutes a speech problem, what to do about it, or where to refer it. To help the doctor to give adequate advice to the family with a speech problem, the following discussion is presented.

Normal Development of Speech

In order to understand when speech is deviating from the normal and the nature of the deviation, it is necessary first to understand the normal development of speech. With an understanding of how speech develops, it is not difficult to evaluate the speech of a child by the time he is a year old. At any particular age thereafter it can be determined when the development is abnormal to a degree that constitutes a problem.

In assessing the prelanguage development of a child in its first year, one needs to be aware of how the child vocalizes, what sounds he makes, how he begins to combine sounds, when and how he develops vocal variety (inflection), when he begins to imitate, and when and how he responds to spoken sound. Between the ages of 1 and 6, children quite consistently follow a general pattern in development of expressive speech, comprehension of speech, articulation of sounds, general intelligibility, and sentence structure. The language development charts in tables 1, 2, and 3 show, in abbreviated form, the normal pattern of language development from birth to age 6. Some deviations can be expected at times and should be taken into account. Unusual deviations may indicate trouble and the necessity to do something about it.

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Critical Periods in Speech Development

Many parents and some doctors appear to feel that the first year of a child's life is relatively unimportant with respect to the growth and development of language because little speech appears The fact is, however, that this period is extremely important. A great deal of prelanguage activity takes place from the time the child begins actively to babble, at the age of about 4 months, until he begins to use his first words some time between 9 and 12 months. The babbling appears to be a rehearsal for the first words. It is that period in which the child learns to enjoy hearing and making a variety of vocal sounds. Because he enjoys this activity, he does a great deal of it. In so doing, he makes many different sound combinations, which provide some valuable ear training as well as exercise of the speech organs.

TABLE 1—*Pattern of Normal Language Development in Vocalization and Response to Vocal Sound*

Age, Mo	Vocalization	Response to Vocal Sound
1	Crying, whimpering, produces some vowels and consonants, k, g, h Sighs, grunts, explosives	
2 and 3	Pitch of crying slightly higher More noncrying vocalizing Different kind of crying for pain, hunger Some repetitive vocalizing, "gagaga' Adds m, ng	Sometimes smiles or is soothed by pleasant adult voice Responds to adult cooing by repeating own formerly practiced sounds Sometimes stops vocalizing when adult joins in May cry in response to angry voice, coo, sigh, gurgle in response to pleasant voice
4	Babbling and vocal play begins, repetitive vocalizing—mostly when child is alone Begins to use consonants m, k, g, p, b, ng, and most vowels Smiles, laughs, gurgles, coos when comfortable	Imitative response to speech decreases and does not reappear until about the ninth month Indiscriminate interruption of babbling causes child to stop vocalizing
5	Increase of above Occasionally responds to parental babbling if done softly and not interrupting child's vocal play	Responds to voices by turning eye and head Automatic response to friendly or angry tone Vocalizes displeasure at losing toy, etc
6	More repetitive babbling, with marked rhythm Increase in intensity from whisper More noncrying sounds Nasal tone begins to be heard Some tongue tip activity begins	Response to friendly or angry tone not automatic but depends on other aspects of the situation gestures, physical contact
7	More variety Dissyllables Same sounds repeated several days Adds d, t, n, w to babbling	Mostly rejects demands for imitation of sounds Responds to gestures accompanied by voice
8	Begins to imitate own vocal play, "mama," "dada," "baba' but not in response to adults Babbling shows pitch and inflection change Increased tongue tip activity	Calls for attention Combines babbling with gestures Perseverates in imitating hand clapping, etc, accompanied by voice
9	More variety in crying and babbling, more back vowels used Higher pitch and more pitch variation Crys to get attention More of vocalizing is babbling rather than crying	Retreats from strangers and mostly from other children by crying Holds out arms to be picked up if adult does the same Not much imitative response to accompanying vocalizing
10	Makes effort to imitate others Can imitate if adults use same sounds as in child's vocal play May use one word correctly	Begins to comprehend no no," 'dada' Will respond to words 'patty-cake, 'bye bye," with gestures
11	Can imitate correct number of syllables and sounds heard in adult vocal stimulation Imitates some new sounds not previously used	Shows interest in isolated words associated with objects or activities important to the child Will imitate two tones sung by an adult
12	Some echolalia if sounds introduced unobstrusively by adults Accompanies vocalization with gestures May acquire first true word(s) Much interest in isolated words connected with own needs and activities	Sometimes will imitate dogs, clocks, cows, or adult exclamations Imitates adult words with initial sound(s) 'Pup' —"p' or "pu' Often imitates dissyllabic words

Because baby enjoys playing with sounds, others around him join in the fun and repeat the sounds back to him. Mother is likely to take her cue from the baby during this period and babble with him Through this method he comes to know that the making of sound has an effect on others. He begins to use it for this purpose. At this point, usually 9 to 12 months, he will begin to vary his pitch, inflection, and volume to suit particular needs. At the same time, he will be making combinations of sounds that begin to sound like words. In this manner, the combination "mama" usually appears. Mother hears it and usually comes to baby, repeating "mama" after him several times. It does not take long for baby to learn that repetition of this particular combination of sounds will satisfy many of his needs. Other words develop in the same way, and a vocabulary is begun.

Normal development of language can be interrupted in the first year by events that might interfere with baby's vocal play and prelanguage activity. Prolonged or serious illnesses, congenital malformations, birth trauma, delayed general development, mental retardation, or inadequate hearing may affect the child in such a way as to prevent babbling and the enjoyment of prelanguage activity. Emotional trauma, even during the first year, also can interfere with language development. The lack of a mother, or a mother figure, in close rela-

TABLE 2—*Pattern of Normal Language Development in Articulation and General Intelligibility*

Age, Yr	Articulation	General Intelligibility
1 2	Uses all vowels and consonants m, b, p, k, g, w, h, n, t, d Omits most final consonants, some initial Substitutes consonants above for more difficult Much unintelligible jargon around 18 mo Good inflection, rate	Words used may be no more than 25% intelligible to unfamiliar listener Jargon near 18 mo almost 100% unintelligible Improvement noticeable between 21 and 24 mo
2 3	Continues all sounds above with vowels but use is inconsistent Tries many new sounds, but poor mastery Much substitution Omission of final consonants Articulation lags behind vocabulary	Words about 65% intelligible by 2 years, 70-80% intelligible in context by 3 Many individual sounds faulty but total context generally understood Some incomprehensibility because of faulty sentence structure
3-4	Masters b, t, d, k, g, and tries many others including f, v, th, s, z and consonant combinations tr, bl, pr, gr, dr, but r and l may be faulty so substitutes w or omits Speech almost intelligible Uses th inconsistently	Speech usually 90 to 100% intelligible in context Individual sounds still faulty and some trouble with sentence structure
4 5	Masters f and v and many consonant combinations Should be little omission of initial and final consonants Fewer substitutes but may be some May distort r, l, s, z sh, ch j, th No trouble with multisyllabled words	Speech is intelligible in context even though some sounds are still faulty
5-6	Masters r, l, th, and such blends as tl gr, bl br, pr, etc. May still have some trouble with blends such as thr sk, st, shr May still distort s z, sh, ch j May not master these sounds until age 7½	Good

tionship with the child often seriously retards the development of speech. It is interesting that most children seem to have to go through the various stages of language development, including the early prelanguage period, no matter how late they start to talk. Even a 4, 5, or 6 year old who has had no speech often will begin, if he begins at all, by babbling. For this reason it is essential that the first year be conducive to normal prelanguage activity if later language functions are to develop according to schedule.

From the age of 12 to 18 months little obvious language development takes place. The child seems to be too busy learning to walk and to physically explore his immediate environment to be concerned with verbal explorations. During this period speech sometimes comes to a virtual standstill. Parents may become quite alarmed at this change and want to know the reasons for it. Normally, around 18 months the child's language begins to develop rapidly. From 15 to 20 words at 18 months, the expressive vocabulary may jump to 250 words by the time he is 2 years old. Some time during this period the child will pass through the "jargon stage" in which his speech will sound very much like normal well-inflected conversation, except that almost none of it is intelligible. This stage seems to be a rehearsal for the connected speech which should begin about the age of 2. Parents sometimes are alarmed at this 18-month jargon and think that something has gone wrong with the child's speech. They can be assured that he will pass through this stage quickly to the next one, in which he will begin to use connected speech in partial sentences such as "Go bye bye," "Baby go," "Daddy come."

TABLE 3.—*Pattern of Normal Language Development in Expressive Speech and Comprehension of Speech*

Age, Yr.	Expressive Speech	Comprehension of Speech
1-2	Uses 1 to 3 words at 12 mo., 10 to 15 at 15 mo., 15 to 20 at 18 mo., about 100-200 by 2 yr. Knows names of most objects he uses. Names few people, uses verbs but not correctly with subjects. Jargon and echolalia. Names 1 to 3 pictures.	Begins to relate symbol and object meaning. Adjusts to comments. Inhibits on command. Responds correctly to "give me that," "sit down," "stand up," with gestures. Puts watch to ear on command. Understands simple questions. Recognizes 120-275 words.
2-3	Vocabulary increases to 300-500 words. Says "where kitty," "ball all gone," "want cookie," "go bye bye car." Jargon mostly gone. Vocalizing increases. Has fluency trouble. Speech not adequate for communication needs.	Rapid increase in comprehension vocabulary to 400 at 2½, 800 at 3. Responds to commands using "on," "under," "up," "down," "over there," "by," "run," "walk," "jump up," "throw," "run fast," "be quiet," and commands containing two related actions.
3-4	Uses 600-1,000 words, becomes conscious of speech. 3-4 words per speech response. Personal pronouns, some adjectives, adverbs, and prepositions appear. Mostly simple sentences, but some complex. Speech more useful.	Understands up to 1,500 words by age 4. Recognizes plurals, sex difference, pronouns, adjectives. Comprehends complex and compound sentences. Answers simple questions.
4-5	Increase in vocabulary to 1,100-1,600 words. More 3-4 syllable words. More adjectives, adverbs, prepositions, and conjunctions. Articles appear. 4,5,6 word sentences, syntax quite good. Uses plurals. Fluency improves. Proper nouns decrease, pronouns increase.	Comprehends from 1,500 to 2,000 words. Carries out more complex commands, with 2-3 actions. Understands dependent clause, "if," "because," "when," "why."
5-6	Increase in vocabulary to 1,500-2,100 words. Complete 5-6 word sentences, compound, complex, with some dependent clauses. Syntax near normal. Quite fluent. More multisyllable words.	Understands vocabulary of 2,500 to 2,800 words. Responds correctly to more complicated sentences but is still confused *at times* by involved sentences.

The period from age 2 to 4 probably is the most critical with respect to language development. In this period the child makes a great effort to use his rapidly increasing, but very new and inadequate, vocabulary to meet his growing needs—and also to conform to a very confusing language environment. Often he finds himself without words at his command, so he does as any of us do in such a situation—he hesitates, sometimes backs up, sometimes repeats or fills in with "ah, ah, ah" or "I, I, I, I," and occasionally he will really block and give up the attempt to speak at that particular moment. This situation sometimes results in considerable nonfluency, which is quite normal for many children at this age. It appears much more readily, and usually lasts longer, in boys than in girls. Normally, if the speech is left alone, a child should pass through the worst of the nonfluency in about six months, but some will take from one to two years.

The danger in this situation comes not from the fact that the child is nonfluent but from the fact that adults—and sometimes other children—become disturbed and begin to treat the nonfluency as a problem. Adults often are ready to label this kind of speech as "stammering" or "stuttering." Once they do, they begin to treat the child according to the label. From here on they rapidly make a problem for him. They do this by such admonitions as "slow up," "stop and start over again," "don't talk so fast," "now think what you are going to say." Adults more unwise than this will even scold the child for his nonfluency, while some go so far as to punish him because he "doesn't talk right."

Usually it is during this period that the parents become worried and come to the doctor for help, with some such statement as "My Johnny is stuttering (or stammering). What shall I do?" Generally, the doctor's advice here has been good, in that he has told them to leave the speech alone. The parents, however, often are too disturbed to take this advice unless they have an adequate explanation of why they should leave the speech alone and how to leave it alone. It will help a great deal if the doctor can give them this explanation. The parents need to understand that this is a normal stage of speech development and that too much interference with it—even though the parents are trying to help—may result in a real speech problem. It would be well, too, if the parents and doctors did not label this nonfluent speech as stuttering or stammering. It can be described as "developmental nonfluency" or some other term that is not so fearful to parents.

Between the ages of about 3 and 6 years, a common hazard to the child's speech is that of parents, and others, expecting too much from him as far as the articulation of sounds is concerned. It is not uncommon for parents to become quite disturbed if the 3, 4, or 5 year old is not using the r, l, th, s, z, sh, ch, and some consonant combinations correctly. A glance at the preceding language development chart will show that these sounds all normally develop after age 5, and the last four may not be mastered until age 7. The danger in this situation is the possibility of pressuring the child to produce these sounds and others ahead of schedule and often before he is ready to produce them. Problems of reverting to baby speech, stuttering, and dyslalia sometimes result from this kind of pressure. The doctor can be most helpful here by informing parents as to the normal sequence of sound development and encouraging them to be patient and give the child time. The doctor should, however, know which sounds are in question and whether there is a problem. One of the pamphlets for parents might be suggested to parents with this kind of a question.

By the time a child is ready to start school, his language generally is adequate for most situations. A few children, however, have not gained sufficient stability in the use of language by the time they start school. They suddenly find themselves among 30 or 40 strange children and a strange adult. The language that previously has served them well among their family and a few friends now may be inadequate to cope with the much wider demands. The child again may become nonfluent just as he did during the earlier stage. Many cases of stuttering seem to have begun during kindergarten or first or second grade. The situation is exactly the same, and should be handled the same, as in the 2 to 4 year period. The nonfluency should not be labeled. The child should be given as much security and as little stress as possible while he is given time for his language to mature.

Another danger also is present at this period. Many children are not quite mature enough, in language behavior and in the use of the articulators, to be able to pronounce all sounds clearly by the time they start school. Actually, some do not achieve this maturity until 7 or 8 years of age. Many parents and teachers, however, become quite disturbed if the child is not producing all sounds correctly by the time he is ready to enter school. In order to get the child ready for school, they may begin to "help" him, to correct him, nag at him, and in other ways make a problem where there was no problem. The doctor can encourage the parents to give the child time to mature without expecting more than he is capable of producing. Of course there are speech deviations at any age which are not of a developmental nature and should have attention. The doctor will need to know how to recognize these and deal with them.

Deviations from Normal Speech

The speech pathologist thinks of a speech disorder in terms of its probable origin; either as organically caused or one that he calls functional (with no apparent organic cause) or a combination of both. These disorders usually are thought of as falling into one or more of four areas: 1. Articulation is the production of sound and sound combinations. Deviations in articulation account for from 50 to 70% of all speech disorders. 2. Stuttering (or stammering) accounts for about 25% of all speech problems and usually is broken down into primary and secondary stages, the latter being the stage at which the individual himself considers his nonfluency to be a serious problem. 3. Voice includes about 10% of all speech disorders, and refers to the processes of phonation and resonation and includes deviations of pitch, quality, or volume. 4. Symbolization refers to a language disturbance most usually called "aphasia" or "dysphasia." It is the inability to associate meaning with language symbols in a normal manner. It is thought that from 2 to 4% of speech problems may fall into this category.

The speech pathologist, in his diagnostic report, often will use other terms such as delay (one or more aspects of language, such as articulation, vocabulary, or structure, has not developed according to chronological age); dyslalia (articulation disorder due to structural anomalies or impaired hearing or "functional" causes); dysarthria (articulation disorder due to central nervous system damage affecting speech organs); dysphonia (disorder of voice quality, pitch, or volume); dysphasia (defined under "symbolization" above); rhythm (stuttering, stammering, or cluttering); hypernasality (too much nasal resonance); and hyponasality (too little nasal resonance).

Conditions Which Commonly Cause Speech Disorders

Late Physical Development.—Late physical development may cause retarded coordination and faulty function of the speech organs and two kinds of speech problems: (1) a delay in developing intelligible speech; and (2) articulatory distortion which may or may not follow the retarded speech pattern. In such cases, it is essential to establish the child's general developmental age. Speech therapy applied too early, for the late-developing child, might cause emotional problems and do little to remove the speech defect. Usually best results are obtained from speech therapy when the child is functioning mentally and physically at about a 4-year level.

Dental Misalignment and Malocclusion.—Dental misalignment and malocclusion are most likely to cause articulation problems such as distortion of the sibilant sounds, particularly s and sh. Correction of the structure by an orthodontist is the most direct remedy, but speech therapy often is needed immediately after the structure has been corrected.

Cleft Lip and Palate.—The problem of cleft lip and palate is generally threefold: 1. There is likely to be a retardation because the consonant sounds (p, b, t, d, k, g) needed by the child to establish his early vocabulary are the ones most disturbed by the open palate. Because of this, much of the prelanguage activity is omitted and early vocabulary and sound discrimination are faulty by the time the palate is closed. 2. With a soft-palate cleft, there is generally a hypernasal quality, even after surgery, due to insufficient closure in the velar-pharyngeal area. 3. Often there will be an articulatory problem caused by dental malformation or by faulty tongue placement which develops before the palate is closed.

Early counsel and instruction in speech development are essential for the parents of children with cleft palate. The speech pathologist should see the child and his parents within the first four months and about every six months thereafter for the first two years. It has been found that most of the delay in speech can be prevented under such a program. The original palate surgery sometimes is adequate to prevent hypernasality, but there is not always a close relationship between the length and flexibility of the palate and the degree of hypernasality. It has been found that a small nasopharyngeal leak will produce as much hypernasal quality as a large opening. "Pharyngeal flap" and "pushback" surgical procedures have been found effective in many cases. Dental intervention often can remove articulation problems due to faulty dental structure. Speech therapy, if needed, generally is desirable when the child with a cleft palate is about 4 years of age.

Complete or Partial Paralysis of the Speech Or- · · s.—This condition may result from any disease accident causing injury to the central nervous ystem. The speech problems are likely to be faulty articulation, inadequate voice quality, inadequate pitch, rate, or volume, or any combination of these. With this kind of problem the speech therapist can achieve best results in cooperation with the family doctor, the physical therapist, and the occupational therapist. In children with poliomyelitis it also is extremely important that the retraining program begin as soon as possible after the attack. The first six months appear to be the most critical as far as making adequate progress in speech is concerned. Therapy often must continue over a long period of time, and frequently the therapist must be satisfied with a minimum of progress. It has been found that from 50 to 60% of children with cerebral palsy will have severe speech problems. They are most common in the athetoid and are often accompanied by hearing loss, but the prognosis is usually quite good if the athetosis is not too severe.

"Brain Damage."—As used here the term "brain damage" is limited to central nervous system lesions in areas of the brain most directly affecting language functions and behavior. This kind of damage is associated with what has been called a "brain damage behavior syndrome," which is characterized by hyperactivity, disinhibition, catastrophic reactions, and generally deficiency in language and number concepts.

Speech problems resulting from brain damage, which may not be physically crippling, usually show a disturbance of the language-symbol association function. The most common result is an expressive (sometimes called motor) aphasia, in which the child can understand language but cannot reproduce it. More severe is the receptive (sometimes called auditory) aphasia, the inability to perceive and interpret language symbols. Often there is a combination of the two, called mixed aphasia. Most severe is global aphasia, in which both receptive and expressive areas are completely defective, and there appears to be no "inner language." In mixed and global aphasia all of the language functions are damaged and, if the child develops language, not only will his articulation be faulty but his language structure, vocabulary, and ability to read and write also are likely to be faulty. It is impossible to locate exactly a lesion in the brain from the type of language behavior observed. It is known, however, that a lesion in the left hemisphere generally will be found when the language function has been seriously interfered with. A lesion in the right hemisphere only rarely produces an aphasic condition. It sometimes is found that a major right hemisphere lesion, with some probable damage extending into the left hemisphere, will cause aphasia. It is fairly well established that expressive aphasia comes most often from a lesion in "Broca's area" in the frontal lobe of the left hemisphere. Reading, writing, and visual perception deficiencies also can be localized to about the same extent.

Considerable progress has been made in understanding aphasia in adults, but less is known about what seems to be a similar condition in children. It is felt that many children fail to develop language as they should because of brain lesions that have been undetected but probably were present at birth or occurred in early childhood. A number of children learn to communicate orally with fair adequacy, but unusual language dysfunction begins to show up when they try to learn to read and write in school. Some of these problems can be traced back to brain lesion. Therapy for either verbal or written dysphasia is an extremely complicated procedure, and the prognosis is always open to question. Excellent results have been obtained, however, in a number of cases. Adequate diagnosis is difficult and requires an experienced team of specialists but is of paramount importance.

Mental Retardation.—Mentally retarded children often present a picture of retarded language development with the retardation showing in all areas of language. This generally varies with the intelligence level, however. Children whose intelligence level falls within the 80 to 90 IQ range are likely to develop adequate language unless other retarding factors such as physical and psychological problems are present. When the IQ level is between 70 and 80, it is not uncommon to find retardation in several areas of language. It has been found that most children with IQ's below 70 will develop language which is noticeably deficient in all areas. Improvement in language for the mentally retarded usually is a developmental and maturational process rather than a problem of therapy, although therapy may be justified in some cases. Parents, however, often feel that if the child "could just talk better" he would be all right. Consequently they insist on speech therapy or some other "treatment." The doctor can do much to help the family understand the nature of this problem.

Hearing Loss.—The nature of the speech disorder resulting from hearing loss depends largely upon the amount of loss and the child's ability to cope with it. Deafness or near deafness will cause a great delay in developing language, and faulty articulation, inflection, and pitch patterns will be present when it does develop. Less severe hearing loss is likely to result in articulation problems, particularly with respect to the high frequency sounds, the voiceless sounds, word endings, and sometimes initial consonants. It is not difficult to detect severe hearing loss, but the child with a borderline hearing loss often suffers from a misunderstood speech or behavior problem. In this child the loss is great enough to distort or eliminate many sounds but is not severe enough to be detected by the doctor or the family unless audiometric examination is done. The child often seems to respond normally to a watch tick and other kinds of noises. He hears spoken sound and responds to it, but he cannot distinguish many of its components. Treatment of the speech problem due to hearing loss should start with medical treatment of the cause if it can be treated. If it cannot be treated medically, the child may need amplification, auditory training, and lipreading.

Tonsils and Adenoids.—Enlarged tonsils and adenoids rarely cause speech problems. Occasionally there will be a temporary denasal quality brought about by excessively enlarged adenoids. This usually will disappear as the adenoid mass becomes smaller. Removal of tonsils and adenoids rarely helps to eliminate a speech problem. The critical aspect with respect to infected tonsils and adenoids is the possible damage to hearing. Removal should be considered on the basis of this possibility and the effect on general health rather than as a procedure to improve a child's faulty speech.

"Tonguetie."—Parents almost universally think a child is "tonguetied" when they find a speech problem of any kind. While it is true that a very short lingual frenulum can interfere with the formation of some consonants and clarity of articulation in connected speech, this condition is rarely the only cause of a serious speech disorder. When the child has trouble with articulation and is also found to have a short lingual frenulum, his speech generally can be improved more rapidly if the frenulum is clipped. A speech pathologist generally can tell, by phonetic analysis of the speech, how much the tongue is limited in speech by the short frenulum.

Psychological Problems.—Severe emotional trauma, rejection, overly severe discipline, extreme fear, lack of a mother figure in early years, and such factors often result in major speech problems. Stuttering is one of the results of this kind of problem. Severe sustained emotional upset in the very young child or parental deprivation often will result in marked retardation in speech and sometimes complete lack of speech long beyond the age when it should have appeared. These conditions also may result in voice and articulation disorders when speech does develop. Psychiatric treatment often is indicated before speech therapy is attempted.

Environmental Conditions.—Such environmental conditions as the child's having been abandoned and brought up in a nursery away from a mother figure may cause speech delay. A major speech deviation in a parent or an older sibling may be imitated by a younger child. Specific kinds of voice quality, faulty language structure, and deviations in pronunciation are all known to be imitated by children. Lack of motivation for speech in a home may cause a child to delay the beginnings of speech. The appearance of a new baby, displacing the next youngest child as the central figure, or displacement for some other reason, may result in the displaced child reverting to baby-talk which may become a problem if not handled properly. Treatment of problems caused by environmental conditions often involves removing causes if possible. Sometimes therapy is needed, but removal of the cause often will restore adequate speech.

A Brief Guide for Checking Speech

The doctor should be concerned about the child's speech when any one or more of the following conditions exist: 1. The child is not talking at all by age 2. 2. Speech is largely unintelligible after age 3 3. Sounds are more than a year late in appearing, according to developmental sequence. 4. There are many omissions of initial consonants after age 3. 5. There are many substitutions of easy sounds for difficult ones after age 5. 6. The child uses mostly vowel sounds in his speech. 7. There are no sentences by age 3. 8. Word endings are consistently dropped after age 5. 9. Sentence structure is noticeably faulty at 5. 10. The child is embarrassed and disturbed by his speech at any age. 11. The child is noticeably nonfluent after age 5. 12. The child is

Generally, five terms will be used to designate people working in this field. The term "speech pathologist" usually is applied to individuals holding advanced certification and whose major concern is with pathological speech conditions and the diagnosis of such. The terms "speech therapist" and "speech correctionist" generally are used to designate individuals who do the actual therapy with speech and hearing cases after the diagnosis has been made. In many cases, however, these individuals make diagnoses also. The therapist or correctionist usually holds basic certification in the ASHA or certification from a state or public school district. The term "audiologist" generally designates the same relationship to the field of hearing as speech pathologist does to speech. The term "audiometrist" is used in many areas to designate an individual trained to give audiometric tests but not to interpret or to give therapy. None of these designations are fixed and often they are interchangeable. Many persons hold certification in both speech and hearing and many therapists, pathologists, and audiologists do both diagnosis and treatment in both areas.

A number of state departments of education certify speech and hearing therapists. In general, state requirements are roughly equivalent to those for basic certification in the ASHA. This means that most public school therapists are qualified to give therapy to the more routine kinds of speech problems, and most of them are well enough trained to know when they find a problem that they should not try to handle without help from someone with more training. Often they are not sufficiently trained experienced to diagnose the more complicated lems.

Vhen the doctor wishes to refer a patient for diagnosis, and therapy if it is needed, it is easy for him to check on the qualifications of the clinic or the individual to whom he is referring. If a person is practicing speech therapy in a public school system, he probably is certified by the state's Board of Education. This means that he can give help with the less severe kinds of problems; he should not be asked to make complicated diagnoses. In some situations, school districts have required persons who have inadequate training to diagnose and give therapy for all kinds of problems. Sometimes parents, school officials, and family doctors are somewhat dismayed at the results. The therapist, in this case, is not to be blamed, but his situation should be understood. Outside of the public schools it may be a little more difficult to check on qualifications, but most legitimate speech and hearing specialists will hold active (not associate) membership in the American Speech and Hearing Association and will be listed in its annual directory, which is published in the *Journal of Speech and Hearing Disorders*, as holding either basic or advanced certification. This directory is available at most college and university clinics or at the office of the Executive Secretary of the American Speech and Hearing Association, 1001 Connecticut Ave. N. W., Washington 6, D. C.

As in all professional fields, there are practitioners in speech and hearing who are not qualified and who take advantage of people's disorders for financial gain. It has been easy for these people to practice in the field of speech and hearing because there has been no legal way of restraining such practice. Quackery of this sort usually has centered around the major speech disorders, such as stuttering, and pathological problems, such as cleft palate and cerebral palsy. In the field of hearing the greatest abuse occurs in connection with audiometric testing and the selling of hearing aids. There are, however, a number of private speech and hearing specialists and individuals in private clinics practicing on an ethical and sound basis. These, almost without exception, will be found to be certified by the ASHA. The doctor would render a professional service if he checked this certification before giving support to the unqualified person by making referrals to him.

The doctor could be especially helpful to patients with hearing loss if he could counsel them to have the hearing evaluated by a trained audiologist. When a hearing aid is thought to be needed, the child should be evaluated and the most useful hearing aid fitted at a speech and hearing clinic where there is a trained audiologist who will try several kinds of hearing aids. The ASHA specifically separates the selling of hearing aids from the evaluating of hearing and fitting of hearing aids. To combine these two functions is not considered ethical. Many patients are left at the mercy of high-pressure salesmen if they are not counseled as to how best to obtain the proper hearing aid.

Any modern doctor realizes that the day is past when he can be expected to supply all the answers to questions about any complaint from his patients. He will also be aware, however, that many of his patients and patient's parents still expect this of him. If both he and the speech specialist will make an effort to open the avenues of communication and cooperation between them, it will be a step toward the sharing of at least one problem area and thus easing an unreasonably heavy burden for the doctor.

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COUNCIL ON FOODS AND NUTRITION

Report to the Council

The Council has authorized publication of the following report. This article is part of a nutrition education program which is assisted by the Nutrition Foundation, Inc.

PHILIP L. WHITE, Sc.D., *Secretary.*

DIETARY TREATMENT OF ADULTS WITH DIABETES MELLITUS

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Although dietary measures for the treatment of diabetes mellitus have been used for over a century and a half, uncertainty exists in the minds of many physicians today concerning the therapeutic role of diet in diabetes. Professional uncertainty is often combined with an inability to initiate and to supervise properly a suitable diet. Experience and judgment are needed to promote the dietary habits conducive to control of diabetes within the framework of the patient's everyday life.

Prior to the availability of insulin, diabetic diets were generally high in fat and protein but restricted in carbohydrate and total calories. In more severe cases, periods of complete fasting were used to prolong a precarious existence. The early insulin era was characterized by a gradual liberalization of diet restrictions, with increasing carbohydrate intakes. Normal caloric allowances replaced the semistarvation diet of former times. At present, many physicians employ diets for diabetics that differ little in composition from those of the general nondiabetic population.

An extension of this point of view is the so-called free diet, in which a few high-carbohydrate foods are prohibited, and no attempt is made to regulate food intake. The use of such diets has been associated with a much more tolerant attitude toward glycosuria; insulin is used to abort symptoms and ketosis. Many adult patients with normal weight and moderate eating habits can be successfully managed with insulin, without strict dietary regulation. However, a large body of experience attests to the urgent need for careful dietary regulation, especially in diabetics requiring insulin for therapy.

Three arguments can be marshalled in favor of the continued importance of the diabetic diet. First, it is a valuable educational procedure that helps the patient to understand his disease and leads the way to optimal nutrition. Optimal nutrition implies not only the prevention of deficiencies of essential nutrients but the attainment of an ideal caloric balance. Second, a diabetic diet obviates the use of insulin in perhaps 30 to 40% of the diabetic population. Lastly, and most important of all, diabetic diets allow the patient receiving insulin to integrate the dietary intake of carbohydrates with the time course of the insulin preparation used and permit a closer approach to normal glycemia without undue risk of insulin shock.

The Dietary Prescription

An understanding of the average American diet is essential before a physician can intelligently prescribe for a patient. Joslin advises physicians to inquire into their own intake of calories, carbohydrate, protein, and fat and to follow a calculated diet for a period of time. This experience will help the physician understand his patients' problems and will increase his effectiveness as a teacher. In most respects, the Recommended Dietary Allowances of the Food and Nutrition Board of the National Research Council [1] apply to the diabetic patient. There is little evidence for increased nutritional needs for the stabilized, well-controlled diabetic patient.

The caloric requirement of adults depends on many factors such as sex, age, activity, and climate.[2] Experience has taught that the caloric allowances recommended by the National Research Council are about 300 to 400 calories in excess of the needs of many urban sedentary workers. For middle-aged adult diabetics, initial caloric provision of 30 to 35 calories per kilogram of ideal body weight has proved satisfactory. This may be increased to 40 to 50 calories per kilogram in nutritionally depleted or very active young patients. It is worth remembering that mechanization has reduced the physical labor in most occupations and has reduced occupational differences in caloric requirements.

When diabetes and obesity coexist, as they frequently do, restriction of caloric intake is indicated. Weight reduction improves carbohydrate tolerance, and overt evidences of diabetes may disappear entirely. Intakes of 20 to 25 calories per kilogram of ideal weight and lower may be used for weight

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instructions for modifying the "exchange lists" to permit sodium restriction and for bland, low-fiber diets have been prepared recently. These educational aids are a great boon to the physician instituting the dietary treatment of ambulatory patients.

Space does not permit a description and evaluation of other systems of diabetic dietary management. The "exchange lists" have been emphasized because of their more universal use and greater simplicity, but other systems have certain merits that probably warrant their continued use. In one system the carbohydrate content of a standard serving of a given food is expressed in teaspoons of sugar, a unit equivalent to 4 Gm. of glucose. The system provides a flexible means for computing the carbohydrate quota of each meal. The greater freedom of this method seems to be preferred by the patients at Washington University Clinics and Barnes Hospital.

Special Foods and Sugar Substitutes

As the content of diabetic diets has approached the content of the diet of the general public, the need for special diabetic foods has decreased. Canned and frozen fruits present the greatest problem because of the sirup in which they are prepared. Water-packed fruits, both frozen and canned, are now quite widely available and are becoming more equitable in price. Diabetic ice cream, in which sorbitol replaces sugar, has little to recommend its use. The metabolism of sorbitol follows pathways similar to glucose. There is no reason why diabetics on ample caloric diets cannot include a little ice cream in their diet, and provision is made for this in the "exchange lists." A careful scrutiny e label of diabetic candy will usually indicate es of potential carbohydrate. These products also expensive and are usually inferior in taste.

The substitution of fructose for glucose and starch has been recurrently advocated. Support for this practice has been claimed in biochemical studies which indicate that insulin is not required for fructose utilization. The therapeutic gains achieved with fructose given orally are meager because of the active conversion of fructose to glucose in the intestinal mucosa and liver. The dietary use of fructose as a glucose substitute cannot be recommended.

Sugar substitutes such as saccharin and the cyclohexylsulfamates have long been used by diabetics and are without significant toxicity.[8] The contribution of sodium from sodium cyclohexylsulfate to a low-sodium diet may be significant, and the calcium salt is recommended during sodium restriction. The taste acceptance of these products is strikingly varied among diabetic patients. These agents are either added to foods by the user or incorporated by the manufacturer in dietetic foods and low-caloric carbonated beverages. With patients on liberal carbohydrate intakes, there is little justification for not permitting small measured amounts of sugar for sweetening.

Almost all diabetic patients inquire concerning either alcoholic or carbonated beverages. These items provide empty calories and often carbohydrates that complicate diabetic control. If the physician decides that the occasional use of these drinks is not harmful, the caloric content of the beverage should be deducted from the carbohydrate quota. The patient who is receiving insulin should be warned of the peculiar hazards of intemperance in diabetic individuals.

Summary

The control of dietary carbohydrate and caloric intake continues to be an important element in the treatment of patients with diabetes mellitus. The composition of such diets no longer differs greatly from the diets eaten by the nondiabetic population. The ability to distribute the daily carbohydrate intake in different ways permits the physician to overcome the deficiencies of exogenous insulin preparations. The techniques of dietary education have been greatly simplified, and educational material is now available that should improve both hospital and office treatment of this disease.

The following educational material can be purchased from the American Dietetic Association, 620 N. Michigan Ave., Chicago 11, or the American Diabetes Association, Inc., 1 E. 45th St., New York 17: "Meal Planning with Exchange Lists," "Diabetic Diet Card for Physicians," "A. D. A. Meal Plans No. 1 through 9," "Sodium-Restricted Diabetic Diet," and "Bland, Low-Fiber Diabetic Diet."

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Statement of the Council

The Council has authorized publication of the following statement.

PHILIP L. WHITE, SC.D., *Secretary.*

FATS USED AS DRUGS

Reports to the Council on Foods and Nutrition recently published in THE JOURNAL of the American Medical Association have carried such statements as:

> There is little evidence that small amounts of corn oil added to a diet of ordinary foods containing moderate amounts of animal fat will result in a lowering of the cholesterol level, and there is absolutely no evidence that it will affect the regression of atherosclerosis or lessen the likelihood of the development of coronary artery disease.... We should like to affirm that nutritional researches in this important area of health are most promising and we are enthusiastic about them. But, we think that such enthusiasm should be directed toward further research, to get the many answers we do not have, rather than toward suggesting changes in our accustomed diets, when we are not too sure at this time if, or how, they should be changed.[1]
>
> The hypothesis that dietary fats affect atherogenesis, however plausible and appealing, remains unproved.... However, patients with existent or threatening arteriosclerosis may be justifiably advised to eat higher proportions of unsaturated fats.[2]

At approximately the same time as these and related publications appeared, several pharmaceutical manufacturers began to advertise products purporting to contain large amounts of poly-unsaturated fatty acids with or without vitamin B_6 and vitamin E. Thus, these manufacturers quickly provided preparations for the use of the physician who, after studying the subject and his patients, believes that such treatment is advisable. In this way the physician may judge for himself on the basis of published data and the opinions of experts whether he will prescribe one or another of these preparations.

It might be argued that these preparations are unnecessary, as the physician could do as well or better by simple and inexpensive manipulation of the diet. However, since this may be impractical or decided against for other cogent reasons, these pharmaceutical preparations may be a real advantage on occasion. The likelihood of harm arising from their use seems unlikely so far, although it should be emphasized that final proof of harmlessness is not at hand.

Unfortunately, the matter does not rest simply upon the availability of these pharmaceuticals. They are being promoted by campaigns which, in some instances, are excessive by implication. In spite of the fact that present evidence does not justify widespread prescription of these items, the methods of promotion tend toward, or at least tacitly hope for, larger sales. The implication is that these products in some measure will prevent or modify atherosclerosis. As noted previously, this has by no means been proved. It should be reiterated that the advertising fliers and brochures usually do not state but only imply, albeit strongly, such a therapeutic effect. For example, one manufacturer states that his product "is indicated in myocardial infarction, post-myocardial infarction, angina pectoris, individuals from families with a history of high coronary disease" and several others. Another says "to correct hypercholesterolemia, to help minimize the development of atherosclerosis in all patients, especially in male patients with precordial pain, overweight middle-aged patients of both sexes, patients with visibly tortuous superficial arteries, patients with elevated blood pressure." Effective treatment of overweight and obesity with these preparations seems unlikely as they supply nine calories per gram of fat!

There are two methods for overcoming the overzealous activity of these pharmaceutical houses. First, continued education of physicians and medical students in methods of evaluating new pharmaceuticals and in sources of factual information about them is essential. Let it be admitted that, for attractiveness, the quiet black-and-white pages of scientific and professional journals are a poor second to the color-and-design display of advertisers. Yet, perhaps the satisfying feeling of studying a subject and of correlating data oneself, instead of relying upon colorful brochures, is worth the trouble. Second, pharmaceutical manufacturers should be encouraged to reevaluate their advertising literature[3] dealing with the promotion of materials for the treatment of diseases of possible nutritional origin to ensure its accuracy and avoid unnecessary misinterpretation.

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CLEAN RIVERS AND LAKES

THE APPROACH OF summer revives longing for physical activity in the great outdoors. In people who are old enough it may also revive memories, for example, of the Great Lakes as they were 50 years ago, with seemingly endless stretches of clean sandy beach lined with oaks, birches, and pines. The clean stretches are no longer endless. The rivers, too, have changed, and it is now many decades ' ce one could swim without concern in the is River, or the lower Mississippi, or the Ohio. ome rivers, in fact, even the thought of boating ecomes repellent if one begins to picture the consequences of falling into the water.

The problem of polluted rivers and lakes is, of course, not confined to the United States. Its urgency in other countries is illustrated by a recent account of the "appalling" condition of the Tyne Estuary in England.[1] The Northumbrian Angler's Federation called a public meeting at Newcastle to protest against the pollution of the river by waste from industries and untreated sewage from towns. A sample of water was exhibited that looked exactly like ink. "In 1867, it is on record that the Tyne salmon netters took 500 fish on one tide. . . . Today there is not a salmon in the river." While some proposed a preliminary survey, with scientific analyses of the water, others pointed out that an obvious step of great importance could be taken at once without help from any such survey, inasmuch as "the city of Newcastle and its neighboring sanitary authorities discharged a minimum of 11 tons of untreated sewage direct into the Tyne and its lower tributaries every day of the year" so that "sewage plants, not scientific analyses, were the simple answer." It is pointed out that, aside from the million or so of anglers whose needs for recreation are frustrated by this pollution, there are many more millions who fervently desire a "bright countryside of green leaf and clean, well-fed waters."

The ugliness of a polluted river is not just something esthetically offensive. It is the token of something pernicious that threatens human existence. The preservation of normal plant and animal life in our natural waters is not just a matter of sentiment. It is a necessity if human life is to continue as we know it.

For those reasons it is gratifying to note the systematic, constructive efforts that are being made in this country to reverse the trend of pollution and to restore American lakes and streams to something like their original state. An example illustrating the magnitude of the undertaking is furnished by the Ninth Annual Summary (1957) of the Ohio River Valley Water Sanitation Commission.[2] This is a report of an interstate crusade for clean streams, addressed to the governors of Illinois, Indiana, Kentucky, New York, Ohio, Virginia, Pennsylvania, and West Virginia. The problem before the commission is a continuing one, spurred on by the steady increase in the population of the Ohio River valley and complicated of recent years by the appearance of nuclear installations at various points. New, uncontrolled industries spring up. In 1953 there were 1,247 important industrial establishments, 323 adequately controlled; in 1957 there were 1,431 industrial establishments, 717 adequately controlled. The commission scored a substantial gain, in that the number of inadequately controlled industries was reduced. Some idea of the cost of this accomplishment is conveyed by the fact that one corporation alone reported the construction of sewage works costing some 30 million dollars. Industry will continue to be a problem, for the region of the Mahoning River, a tributary of the Ohio, is described as one of the most heavily industrialized areas in the world.

The increasing population is also significant. In 1940, 35% of 7,970,000 people were served by water purification plants; in 1957, 76% of 9,951,000. Here again the purification forces have scored a gain, but not without an effort. The calendar of the commission's proceedings during 1957 contains an instructive instance of trouble with a city whose inhabitants were unwilling, for various reasons, to treat the sewage they were discharging into the Ohio.

The efforts that have been made by various states to save their rivers from pollution could be illustrated by many examples. The federal government has provided grants to states to assist the states in

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1. Is Purity Worth It? editorial, Roy. Soc. Health J. 78: 1-2 (Jan.-Feb.) 1958.
2. Ninth Annual Summary—1957, Ohio River Valley Water Sanitation Commission, Cincinnati, 1957.
3. Wisniewski, T. F.: Water Pollution Control Grants, Wisconsin M. J. 57:140 (March) 1958.

meeting the cost of adequate measures.[3] Local pride is an important consideration especially when a river like the Wisconsin or the Illinois lies entirely within the borders of the state; its inhabitants have nobody else to blame if the river becomes a disgrace to them. Moreover, the headwaters of rivers have become so important not only in recreation but also in flood control that any proposal to convert them into purely industrial areas must be viewed with great concern. A timely example is the current exploration for copper in the region of the Namekagon, Yellow, and Totagatic rivers in northern Wisconsin. The appearance of mines and smelteries there may prove to be as valuable to the people of Wisconsin as the development of the iron-bearing areas of Minnesota has been to the people of that state. At this stage the local authorities are in a position to bargain with the mining companies. *Many hope the authorities will insist from the beginning* that the companies incorporate in their fundamental planning every precaution against the spoiling of the surrounding territory. This great region of marshes and lakes supplies a steady flow to its rivers throughout the summer, and the result in the past has been quite different from the calamitous alternation between flood and drouth seen in many other parts of the country. With due planning, it should be possible not only to guard against future pollution of the air and water but also to preserve these other values of a beautiful region.

It would be a pity if Americans ever became insensitive to the romance that abides in names like Susquehanna, Delaware, Colorado, St. Croix, Hudson, Columbia, Potomac, Missouri, and Cumberland. Every step toward the restoration of America's grand streams to their original clean magnificence will be the outward token of a vast improvement in the way of life for 170 million people.

CHEMICAL TESTS FOR INTOXICATION—"IMPLIED CONSENT" LAWS

Ever since 1939, when the first statute was enacted in Indiana specifically permitting the use in evidence of the results of chemical tests for intoxication, both prosecuting attorneys and defense attorneys have been concerned with the attitude of the courts toward the constitutional issues involved. Primarily, these issues have related to problems of self-incrimination, search and seizure, and due process of law. Proponents of the use of chemical tests have been diligently seeking some method whereby a properly conceived statute could obviate the subsequent raising of these questions in court.

As early as 1942 the American Medical Association considered the possible utilization of existing state drivers licensing laws as a mechanism for obtaining the necessary consent to the performance of the test on persons suspected of driving while under the influence of alcohol. Inquiry was made into the possibility of conditioning a person's privilege to use the highways in his state upon his promise to submit to a chemical test whenever the need arose. At that time it was felt that such a law was of doubtful constitutionality. Exploration of the idea continued, however, and in 1953 the state of New York enacted an "implied consent" law.

After later amendments to satisfy constitutional objections the law provides that any person who operates a motor vehicle in the state of New York shall be deemed to have consented to a chemical test any time a police officer has reasonable grounds to suspect that he is driving in an intoxicated condition. If the driver then refuses to submit to a test his license to drive shall be revoked. The law as amended has been upheld by the highest court of the state of New York against charges of unconstitutionality.

Similar legislation has since been enacted by the state legislatures of Idaho, Kansas, and Utah.

Last November the Committee on Medicolegal Problems heard a report on "implied consent" laws from its Subcommittee on Chemical Tests for Intoxication. As a result of this report, the Committee recommended to the Board of Trustees that the American Medical Association endorse uniform state legislation patterned after the New York law. The request was approved by the Board of Trustees at its meeting in February, 1958. This places the American Medical Association alongside the American Bar Association, the National Safety Council, and the National Conference of Commissioners on Uniform State Laws in the endorsement of uniform legislation patterned after "implied consent" laws.

As has been said by Prof. Fred Inbau of Northwestern University: "The implied consent statute solution to the constitutional law problems regarding chemical tests is an eminently fair and satisfactory one, both as to the state and the accused. It will set to rest the issues of self-incrimination, search and seizure, and due process which have been raised so frequently in the past. Greater progress will then be made in the efforts of law enforcement officers to curb the menace created by the intoxicated motorist."

It is hoped that the endorsement of this type of legislation by the Association will be of help to those state legislatures which are sincerely trying to find some effective means of eliminating, or at least reducing, the high percentage of highway accidents in which alcohol plays an important part.

THE A. M. A. TEAM

One of the most frequent questions received in American Medical Association headquarters is "Since I am a member of A. M. A. by virtue of my county medical society membership, just what do I get out of my affiliation with the parent association?"

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ORGANIZATION SECTION

STATEMENT REGARDING THE HOSPITAL SURVEY AND CONSTRUCTION ACT BEFORE A SUBCOMMITTEE OF THE HOUSE OF REPRESENTATIVES

Mr. Chairman and Members of the Committee:

I am Dr. Julian P. Price of Florence, South Carolina, a member of the Board of Trustees of the American Medical Association, on whose behalf this statement is presented. Accompanying me today are Dr. Willard A. Wright, Chairman of the Committee on Medical and Related Facilities of the Association's Council on Medical Service and Mr. Joseph Miller of the Council's staff.

When the proposed hospital survey and construction act, commonly known as the Hill-Burton Act, was heard before the 79th Congress, it was considered very carefully by the American Medical Association. As a result, the intent and purposes of the legislation received our approval, and the Association has continued to support the law since its enactment. In February, 1956, our Board of Trustees requested the Council on Medical Service to conduct a comprehensive study of the Hill-Burton program. It was our belief that a complete evaluation should be made of the operation and achievement of the program, since its establishment in 1946, in order to determine whether it had accomplished the purposes for which it was enacted and to determine whether its continuation should be recommended. This project was assigned to our Committee on Medical and Related Facilities.

In evaluating the program, numerous sources of information were used. As a result of conferences held in Washington with representatives of the Public Health Service, comprehensive statistical data were obtained. Annual Survey Reports, obtained from every state and territory, were used in an examination of the program's administration and operation. Questionnaires were sent to all state and territorial medical associations and all available related data were compiled and reviewed.

Field surveys of fourteen states, selected to give an accurate cross section, were undertaken by a team of A. M. A. staff research analysts. The states visited were: Arkansas, California, Connecticut, Georgia, Illinois, Iowa, Kentucky, Maryland, Michigan, Mississippi, Montana, New Jersey, Oregon, and Washington. Because of the original emphasis in the Hill-Burton act on aid to rural and low income areas, six rural states were visited. In the states visited, the research staff interviewed over two hundred persons representing government agencies administering the program, members of state hospital advisory councils, individuals in the field of hospital administration, project sponsors, and members of the medical profession.

With your permission, Mr. Chairman, I would now like to ask Dr. Wright to discuss the results of his Committee's study and the recommendations of the American Medical Association resulting therefrom.

STATEMENT BY WILLARD A. WRIGHT, M.D., ON HILL-BURTON PROGRAM

Mr. Chairman, and Members of the Committee:

I am Dr. Willard A. Wright, Williston, North Dakota, Chairman of the Committee on Medical and Related Facilities of the American Medical Association. As Dr. Price has told you, our committee has recently completed a two-year study of the Hill-Burton program. I would like to discuss the recommendations of the American Medical Association from this study.

It is our recommendation that the Hill-Burton program be continued, although we believe that some of its objectives should be re-defined and that several changes should be made in the program in order to render it more effective. It is our conclusion that, with few exceptions, the Hill-Burton construction program has been administered efficiently and in the interests of the public, and that the objectives of the original legislation are, to a large degree, being achieved.

Emphasis now needs to be directed toward construction of facilities for the chronically ill as a part of a general hospital, toward construction of nursing home facilities, and toward the modernization, renovation and remodeling of existing hospitals. To provide this emphasis, it will in our opinion be necessary to give the states greater latitude in establishing priorities and in allocating funds.

Since its inception, one of the objectives of the program has been to give "specific consideration to hospitals serving rural communities and areas with relatively small financial resources." We have found that, for the most part, this objective has been achieved. Of the seventeen states described in the 1950 census as being fifty per cent or more rural, our staff members visited six. These six states had two hundred and thirty-five areas designated as rural. In one hundred and forty of these areas at least seventy-five percent of their hospital bed

First of all, the A. M. A. should not be considered the "parent" organization. More accurately it is the offspring of the 1,915 local medical societies throughout the United States and the American territories. The immediate and obvious answer to the question, however, is that a member of the A. M. A. gains status as a reputable physician, acceptance by his professional colleagues, and recognition of the right to mingle with his colleagues, particularly in their scientific discussions, to work with them for common objectives. In other words, the A. M. A. member becomes a member of the team.

The major purpose of the A. M. A. is to help the doctor help the patient. In return for A. M. A. dues a member receives a membership card that entitles him to a great many services, some direct, many indirect. A few years ago the late Dr. Rock Sleyster, then President of the A. M. A., characterized the association headquarters as a ammunition factory where products were developed for use on the battle line. Some of these products are as tangible as a pamphlet and others, equally important, as intangible as an attitude.

The most complete evaluation and description of A. M. A. services is found in the pamphlet "A. M. A. in Action," which can be obtained from headquarters office. Here all the different bureaus and councils are described and relationships with health agencies and other national health groups are illustrated.

Through studies, research, and surveys by the divisions within the A. M. A. working essentially in the field of medical economics, the association acquires information and sometimes definitive knowle on medical care problems throughout America. s the A. M. A. raises the voice of American edicine in social-medical matters to the same high level it now enjoys when American medicine speaks on scientific medical matters.

American medicine is speaking to the public through the accepted channels of public information—the radio, television, and the press. If we give our community leaders, writers, commentators, officials, and legislators, both state and national, the facts, not propaganda, then they will see for themselves what an active, dynamic medical organization really is doing to safeguard the health and lives of the American public and hence will not permit medicine to become a tool of government and the politicians.

In addition to weekly and monthly publications, the association sponsors two mammoth medical meetings annually, plus special conferences; maintains a package and periodical lending library service; conducts a physician's question-and-answer service; and prepares books and articles, such as New and Nonofficial Drugs, carrying latest monographs on drugs and treatment information.

All the above and much more is made possible only because over 90% of the practicing physicians in the United States want to belong to the same team. To be sure, not all participate in team activities all the time, but the A. M. A. is unique in that there are never any "scrubs"; all are members of the first, and only, team in American medicine.

WHY PEOPLE BOUGHT LIFE INSURANCE

A recent survey of members of 3,000 spending units sampled in a continuing study by the Survey Research Center of the University of Michigan in cooperation with the Board of Governors of the Federal Reserve System indicates that life insurance is purchased for many reasons.[1] Whereas only 12% mentioned insurance as a good method of saving, 35% gave as one reason for paying premiums the establishment of a "clean-up" fund to pay outstanding bills, debts, and funeral expenses. Provision for paying the costs of the last illness is given by life insurance salesmen as one of the major reasons for buying life insurance, and this survey of persons who had purchased life insurance and continued to pay premiums thereon verifies the appeal of this familiar sales argument.

The rapid growth of voluntary health insurance has tended to obscure this time-honored role of life insurance in defraying the costs of the last illness. More than one billion dollars a year is paid out by life insurance companies for death claims of persons aged 65 and over, the age group which experiences the highest mortality rates. The funds made available through life insurance for paying medical and hospital debts for the last illness are just as useful to the surviving members of the family as are the payments made under health insurance policies. One cannot, of course, know which illness or accident will be the last, but the last one is typically the most expensive. This survey also indicates that the proportion of persons in the age group 65 and over owning life insurance increased from 52% in 1950 to 56% in 1956.

Whereas only 18% of the spending units with incomes of $7,500 or more mentioned the provision of a "clean-up" fund as one of the basic reasons for purchasing insurance, 65% of those with earnings of less than $2,000 a year were motivated in part by the desire to provide such a fund. Moreover, it is likely that many respondents who gave "to provide for dependents" as one of the reasons for buying life insurance could have had in mind the advantage to dependents of providing for the payment of debts outstanding at the time of death.

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1. Miner, J. L.: Life Insurance Ownership Among American Families, 1957, Ann Arbor, Mich., University of Michigan, 1958.

We also believe that with the elimination of the specific categories of facilities mentioned we would have a better program and one that will be more effective in achieving the basic purposes of the act.

STATEMENT REGARDING AUTOMOBILE ACCIDENT PROBLEM, BEFORE A SUBCOMMITTEE OF THE HOUSE OF REPRESENTATIVES BY FLETCHER W. WOODWARD, M.D.

Mr. Chairman and Members of the Committee:

I am Dr. Fletcher D. Woodward of Charlottesville, Virginia, where I am engaged in the private practice of medicine and also serve on the faculty of the School of Medicine of the University of Virginia.

I am Chairman of the Committee on Medical Aspects of Automobile Injuries and Deaths of the American Medical Association and am appearing today on behalf of that Association. I would like first to express my appreciation for this opportunity to appear before you to tell you something of what the American Medical Association is trying to accomplish in the field of traffic safety and accident prevention.

The American Medical Association has been concerned with the problem of automobile injuries and deaths for many years. Actions of our House of Delegates on this subject are numerous and date back as far as 1929. In 1948, our House passed the following Resolution:

WHEREAS, The American Medical Association has in the past cooperated with the National Safety Council in its efforts to reduce the incidence of deaths and injuries from accidental causes; and

WHEREAS, The studies that have been made by the Bureau of Medical Economic Research of the American Medical Association have established the fact that fatal accidents cut off more years from the working lifetime of the American people than any one natural cause of death; and

WHEREAS, In the recent report made to the President by the administrator of the Federal Security Agency, it was stated that 40,000 deaths annually from accidents were preventable; therefore be it

RESOLVED, That the Board of Trustees be instructed to cooperate in every possible way with the National Safety Council and with every other agency, both public and private, concerned with accident prevention, to the end that research in accident prevention be further stimulated; that this excessive drain on hospital and medical facilities be lessened, and that the appalling loss of working years be reduced.

For more than 30 years our Association has had Committees actively working on the various aspects of the automobile accident problem. The present Committee was appointed by our Board of Trustees in 1955. Its members are chosen from physicians who by their interest and work were considered to be well qualified in this field.

We believe most people will agree that those who are called upon night and day to pronounce dead those persons killed on our highways, and who mend the broken bodies of those who are injured, can well be classified as interested and qualified in their efforts to prevent such carnage. Within the lifetime of most of us here, we have seen substantial gains by the medical and allied health professions in the conquest of disease and disability. Many of the diseases that were commonplace early in this century have been conquered or brought under effective control. Many diseases that were once widespread are now a rarity. However, accidental injuries and disabilities due to automobile accidents have become the number one public health problem of our time. We believe it is important, therefore, that the medical profession continue to increase its interest in the automobile accident problem until effective improvement is a reality.

As the result of our studies, we are convinced that if speed, recklessness and drunken driving are controlled, and if improvements in automobile design are provided to protect those involved in collisions, then the present appalling toll of injuries can be substantially reduced. We are further convinced that enough facts are at hand to accomplish this purpose now.

My statement will consist of a delineation of the several objectives of the American Medical Association's Committee on Medical Aspects of Automobile Injuries and Deaths, and a discussion of past, present, and planned activities in each case.

One of our most important objectives is to provide the practicing physician with technical medical information which will enable him to advise and inform his patients relative to driving limitations that may be involved in: a. Physiological states; b. Pathological conditions; c. Emotional disturbances; and d. Drugs and alcohol.

We realize that a certain percentage of accidents are undoubtedly caused directly or indirectly by medical conditions, drugs, and other related physical factors and that it should be our first duty to clean our own house. To this end we sponsored a symposium on Medical Aspects of Automobile Injuries and Deaths and presented it at the Association's Annual Meeting in June, 1956, in Chicago. These papers were published in THE JOURNAL, Jan. 26, 1957 issue, pages 225-262. Reprints are available and copies will be furnished to members of your Committee.

Our next objective is to prepare a comprehensive book to serve as a guide to physicians in determining fitness to drive as related to the medical back-needs had been met; fifty areas had met fifty to seventy-four percent of their needs, and only forty-five areas had met less than fifty percent of their bed needs. In these six states, we found that from sixty-two to ninety-two percent of the total federal determination for hospital beds had been met. We also found that in these states the percentage of construction funds allocated to rural areas was showing a definite downward trend. A similar downward trend in allocations for construction in rural areas was also found in the other eight rural states visited.

Therefore, we believe it is logical to assume that in most states, the special need for rural hospitals no longer exists. This was also, generally, the opinion of those persons responsible for the administration of the program in the states visited, and it is substantiated by occupancy statistics. It appears therefore that in a number of states the greatest need for hospital beds is in the metropolitan areas. Existing priority factors, however, have limited such construction. Therefore, it is recommended that mandatory priority for rural areas be abandoned and that the individual states be permitted to establish priorities in accordance with their particular needs.

In order to grant the states greater freedom in allocating funds, we would recommend that all present categorical grants, as set forth in Section 651 of the Act, be eliminated. We would substitute for these categorical grants one single appropriation for all facilities covered under the act, thus allowing maximum freedom of re-allocation.

We have found that federal assignment of specific funds to special projects, such as chronic sease facilities, diagnostic or treatment centers, bilitation facilities, and nursing homes, has ously handicapped worthwhile programs in some of the states. For example, in the case of rehabilitation facilities, rigid assignments have forced some states to lose their allotment to other states. Federal assignment of funds to special-type projects also tends to increase administrative problems because of the built-in inflexibilities.

We would next recommend that the diagnostic or treatment center facility be eliminated entirely from the act. We found much confusion in the states as to what the term diagnostic or treatment centers means. There is little evidence of a need or demand for such a provision to build the ill-defined units. We believe that increases in diagnostic and treatment services for the people are dependent primarily on the availability of medical and para-medical personnel.

When it was proposed to add the diagnostic and treatment center category to the Hill-Burton program, we expressed our doubts concerning the needs of federal grants for such facilities. We also felt that the definition given in the act was vague and ambiguous. Our study has confirmed our doubts with respect to this part of the program.

We would also recommend that the public health center, as a facility, be eliminated from the provisions of the act. Since most states have provided for public health center construction through appropriate local and state tax resources, it is doubtful that the continuation of this phase of the program for the benefit of a few states is justified. We found that fourteen states had 89.4% of the total number of approved public health center projects and received 76.4% of the federal funds allocated to this category. We believe that these facilities can and should be provided by the states or local communities and that federal aid is no longer needed or justified.

Several of the bills now before this committee propose the institution of a loan program under the Hill-Burton Act. The A. M. A. has taken no position on this specific proposal. It is, however, the position of the American Medical Association that a government-insured loan program of the Federal-Housing Administration-type for hospitals and nursing homes, both nonprofit and proprietary, should be approved.

In summary our recommendations are as follows:

1. That the Hill-Burton program be continued.
2. That emphasis be directed toward construction of facilities for the chronically ill as part of a general hospital, toward construction of nursing home facilities, and toward the modernization, renovation, and remodeling of existing hospitals.
3. That priority for rural areas be abandoned and that individual states be permitted to establish priorities in accordance with their particular needs.
4. That categorical grants be eliminated in order to allow the states maximum freedom in their allocations.
5. That the diagnostic or treatment center facilities be eliminated entirely.
6. That the public health center facilities be eliminated entirely.

We are very much aware of experimentation and possible future changes in the effective utilization of hospital facilities. We feel that in any program for the future it will be necessary to examine closely and consider carefully the probability of radical changes in the methods of caring for people in hospitals. There is a distinct tendency to reduce the necessity for the length of stay and for certain highly specialized services available to everyone. These are other reasons why we feel the program should be made as flexible as possible.

In conclusion, I would again like to express the general support of the American Medical Association for the Hill-Burton program and reiterate our conclusion that it has been successful and efficiently administered. We believe that if our recommendations are adopted the states will have greater freedom in establishing priorities and allocating funds for the various facilities currently required.

8. Eliminate sharp, pointed hood ornaments. These fill no functional need and are potentially lethal to pedestrians.

9. Eliminate other hazardous exterior design features such as sharp, pointed bumper ornaments.

In addition, we feel that the automobile industry should make an open-minded examination of other suggestions and adopt them where feasible. For example:

1. Shock-absorbing bumpers; if one drives his car into a brick wall at one mile per hour, he will be astounded at the shock transmitted by such an impact. One person testifying before your Committee intimated that to absorb the energy at 20 miles per hour in a 4,000-pound car, such a bumper would have to be 16 feet long. I am not an engineer, but it seems to me that engineers are ingenious enough to provide practical, energy-absorbing bumpers, especially at the front end, and possibly at the rear as well.

2. Polarized headlight lenses and an oppositely polarized windshield spot; this has been repeatedly suggested and I have yet to see any reasons presented as to why it should not be adopted. It would prevent glare at night and thereby prevent many pedestrian accidents and deaths.

3. Consideration should be given to the design of windshield and rear windows to meet standards based on optical principles.

4. Provide protective side-swipe bumpers along the sides.

5. Provide warning reflectors on the sides

6. Remove tail lights from the realm of the artistic designer.

7. Provide a positive separation of turn signal lights from other lights.

8. Eliminate the glare-reflecting surfaces on the interior.

9. Provide accurate speedometers. Why do we have speedometer dials indicating up to 120 miles per hour? Why not an audible warning device to denote when safe speed has been passed?

10. Construct drivers' seats with better regard for the posture and visibility of persons of various heights.

11. Make chrome, clocks, radiator ornaments and other expensive gadgets optional equipment and install safety equipment as standard equipment.

As evidence of the interest in this subject by the entire medical profession and the conviction that something constructive can and should be done toward the prevention of injuries, I wish to quote a Resolution adopted by the House of Delegates of the American Medical Association at its meeting in Boston on Dec. 1, 1955:

WHEREAS, Traffic accidents in the United States claim 38,000 lives and 1,250,000 injured each year, with a probable 45% increase in vehicle mileage in the next ten years; and

WHEREAS, This death and accident toll could be materially reduced through improvement in automotive safety design and construction; and,

WHEREAS, All other modes of public transportation except automobile are already safeguarded by Federal safety standards; therefore be it

RESOLVED, That the American Medical Association, through its House of Delegates, strongly urges the President of the United States to request legislation from Congress authorizing the appointment of a national body to approve and regulate safety standards of automobile construction.

On Jan. 9, 1956, Dr. George F. Lull, Secretary and General Manager of the Association, addressed a letter to President Eisenhower in which he directed attention to the Resolution.

The next objective of our Committee is to promote the extension of emergency first aid training to as many citizens as possible. This training will be of value not only in connection with the reduction of the severity of automobile crash injuries, but also in connection with civil defense needs as well. We feel it is also desirable that all automobiles be equipped with first aid kits.

Related to first aid is another objective—to assist in the promulgation and to promote the use of standards for organized emergency services in local communities, including training of rescue squads and standardized equipment for rescue vehicles. This is a future activity in which we will work through state and county medical societies. An example of one problem in this area is the need for better selection, education and control of drivers of emergency vehicles. There are cases on record of ambulance drivers speeding and screaming through heavy traffic when carrying a corpse to a morgue.

As citizens and physicians, we recognize the importance of driving courses for all high school students. Similar courses should be provided for the public and the curriculum should meet certain basic educational requirements. We sincerely hope the day will soon come when such certificates will be required of all prospective drivers as well as for repeat traffic law violators.

We intend to invite representatives from all state medical societies to meet with us in San Francisco in June, 1958, at the time of the Annual Meeting of the American Medical Association. At that time, we plan to recommend a uniform group of objectives for the consideration of the state medical societies.

Since speed and driving under the influence of alcohol and their related offenses are intimately associated, we feel that stricter laws than any that now exist on our statute books should be provided. The public needs to be aroused to the point whereby the legislators will provide these laws and the traffic courts will administer them without fear and with complete impartiality.

ground of the individual. When completed, this book will represent a compilation of medical data and the opinions of nationally recognized authorities in the various special fields of medical practice. With this information available, it should be possible for the individual physician to make a significant contribution to the welfare of his personal patients and the public at large.

Closely related to the need for factual information to aid the physician is the need to inform the driving public through use of proper media of the medical conditions which may affect their driving proficiency. We believe that many individuals would voluntarily discontinue or diminish radically their driving if they understood the dangerous possibilities involved in certain physical disorders and the potential effects of certain medications. In other words, if we supplement the technical information furnished the physician with a pamphlet written at the popular level and covering the more commonly encountered medical situations, the patient can have the advantage of something in print which will serve to instruct him as to whether he should or should not drive; and, if so, under what safeguards. It is contemplated that this information as well as the data for physicians will be published in The Journal of the American Medical Association.

There is little doubt that a great deal of attention must be given to the very serious question of who shall be permitted to drive an automobile and who shall be denied that privilege. We emphasize that driving should be a privilege rather than a right. Therefore, our third objective is to develop better medical standards for driver licensing, including preparation of a guide for license examiners and assistance to state agencies concerned with licensing. This will be based on the information compiled in the medical criteria mentioned earlier and will constitute our recommendations for state licensing agencies. We recommend that each state medical society have a committee on traffic safety. Such committees would be in a position to advise and assist state driver licensing bodies in the improvement of medical standards for licensing.

Another objective is to study and report on the design features of automobiles. In improvement of the design and safety equipment of automobiles rests the greatest possibility for rapid reduction in the automobile injury and death toll. If it is estimated that the average life of an automobile is ten years, it is apparent that a very considerable reduction in the severity of injuries and a marked reduction in fatalities could be accomplished in that time, if more attention were devoted to providing safety rather than to increased horsepower, streamlining, color, and chrome.

On the other hand, it will probably take a long time to engineer maximum safety into our major highways. It must also be recognized that on the secondary roads maximum safety in design may never be economically feasible. We would hesitate to forecast how long it will take to inculcate safe-driving practices, attitudes and proficiency into 75 or 100 million drivers.

The engineers and the designers of the automobile—a relative handful of men in the industry—virtually control the destinies of the American public on the highways. They are the men who decide which elements of safety design will be put into or left out of next year's new automobile.

There is presently available an ample body of research data which clearly indicates the definite values of certain safety features of automobile design, construction and equipment. Yet, these safety features are all too often made available as optional equipment at extra cost. The automobile industry can make a great contribution toward solution of this problem by consulting with physicians, anthropologists, psychologists, related biological scientists, and other scientific professions, and by giving realistic consideration to the wide range of physical characteristics of automobile drivers and riders and what happens to them in a collision.

In the past the automobile industry has made many important contributions to safety. However, in recent years, safety has generally been ignored in favor of other developments. The following suggestions have been repeatedly advanced by physicians, researchers, and safety engineers with but little success.

1. Anchorage for seat belts should be standard equipment. The public also needs education in the value of seat belts. The only evidence so far presented against seat belts is in the number of deaths in sports cars during roll-overs. This is not an argument against seat belts but against the design of such cars which do not provide roll-over bars. It should be quite simple to incorporate such a bar in the windshield and a second one back of the seat.

2. Crash padding of the dash, roof, and other areas should be provided.

3. An improved steering wheel and recessed post: perhaps a collapsible assembly—I have been told it could not be done and yet I saw a foreign car the other day that provided such steering assembly.

4. Safety door locks should be standard in all cars.

5. Removal of dangerous knobs, buttons, sharp edges, and other gadgets.

6. Seats should be securely anchored to the floor of the car and should be locked into position. They should also be high enough in the center to protect the neck in a rear-end impact and prevent neck-snap injury (also called whiplash).

7. Eliminate the deck behind the rear seat as a storage place for flying missiles or provide it with an effective retaining rail or construct it as a recessed pocket.

assurances of free choice of physician, actuarial soundness, "the greatest possible scope of benefits (medical expanses of economic consequence) to the subscriber," maximum participation by medical society members, support of medical society policies, safeguards for continued high standards of medical practice, the right of societies to withdraw sponsorship for valid reasons, and proper and realistic contract provisions.

NEW FILM—HELPING HANDS FOR JULIE

A 7-year-old youngster is helping to influence students to choose a career on the health team She is Julie Morgan, star of the new 16-mm medical health career recruitment film produced by the American Medical Association, the American Hospital Association, and E. R Squibb & Sons "Helping Hands for Julie" tells the story of the fight to save Julie's life. The helping hands aiding the doctors in finding the correct diagnosis of meningitis are those of the nurse, medical technologists, x-ray technicians, and medical record librarians. The drugs of the pharmacist, the nourishing food of the dietician, the restorative work of the physical therapist, and the care of the nurses help bring Julie back to health.

Medical societies and auxiliaries may arrange for bookings of this 30-min., black and white sound film through the A. M. A. Film Library after July 1.

A. M. A. TO ENTERTAIN DELEGATES FROM WHO

The American Medical Association will join with four other national groups to entertain delegates to the World Health Assembly after the Assembly's meeting in Minneapolis May 26-June 14. En route home, some 250 physicians, health workers, and medical administrators from 88 countries will travel to Chicago for a two-day stopover.

The A. M. A., together with the American Hospital Association, the American College of Surgeons, the American Dental Association, and the Joint Commission on Accreditation of Hospitals, has scheduled a reception for the delegates Sunday evening, June 15. Among guests, in addition to representatives of the dental, medical, and hospital groups, will be Chicago Mayor Richard Daley and members of the Chicago consular corps. On Monday, June 16, the WHO delegates will take tours according to their special interests. One group will visit A. M. A. headquarters to learn the workings of the organization and meet members of the staff.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

POSTGRADUATE COURSES

Notice of the following postgraduate courses has not previously been published by the Council and is presented for information only

A five-and-one-half-day continuous intensive postgraduate course in **Radioisotopes** will be held at the University of Texas Southwestern Medical School, 5323 Harry Hines Blvd, Dallas 19, June 16-21, 1958, in association with the University of Texas Postgraduate School of Medicine Registration for this course will be $100, and enrollment will be limited to eight registrants Educational methods include lectures, laboratory work and demonstrations, patient demonstration, and clinical conference. Application or inquiry should be addressed to the Division of Postgraduate Education of the University of Texas Southwestern Medical School

A three-day postgraduate course on **Dermatology** will be offered at the University of Colorado Medical Center, 4200 E. Ninth Ave., Denver 20, July 10-12, 1958, primarily for the physician in general practice. Educational methods will include lectures, demonstrations including patients, discussion, and question periods. Inquiries or applications should be addressed to the Office of Postgraduate Medical Education of the University of Colorado Medical Center at the above address.

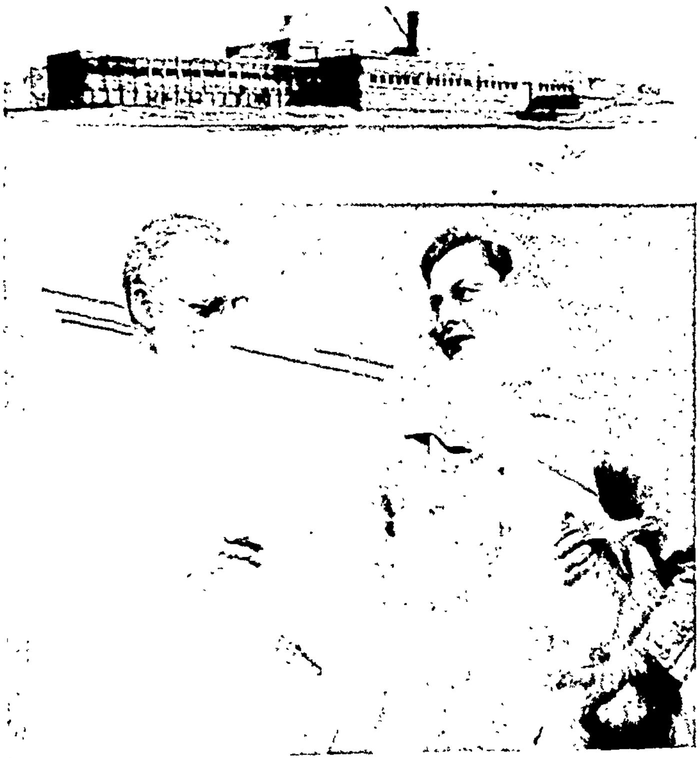
A postgraduate course for industrial physicians and specialists in otolaryngology will be the **Institute on Industrial Deafness** at Colby College, Waterville, Maine, Aug. 10-19, 1958. The eight-day, 50-hour course will have a registration fee of $250 with enrollment limited to 30 persons. Inquiry or application should be addressed to Colby College at the above address.

The University of Puerto Rico School of Medicine, San Juan, will present a nine-month continuous intensive basic science course, for physicians in general practice, on the **Clinical and Research Utilization of Isotopes**, beginning Aug. 15, 1958. The maximum enrollment will be limited to three. at no fee. Educational methods will include laboratory work, patient demonstration, live clinic, bedside rounds, clinical conferences, seminar, lecture, panel discussion, open-question periods, and audio-visual aids, with the registrants having the opportunity of performing procedures. Further information should be obtained from the University of Puerto Rico School of Medicine.

Because of the indefatigable work of many safety organizations over the years, the incidence of death has been greatly reduced in spite of the tremendous increase in the number of vehicles and number of miles traveled. The present figure of 6.4 deaths for 100 million miles traveled is now nearly a static figure. In spite of this apparent success as to the incidence rate, the total number of deaths and injuries is increasing each year. Unless some of the suggestions mentioned above are followed, it seems inevitable that this number will continue to increase each year in spite of all the splendid work now being done.

RESEARCH KENNELS AT GEORGETOWN

The first in a series of projects to furnish more humane quarters for research animals will be dedicated July 1 at the Georgetown University Medical School in Washington, D. C. A volunteer committee of doctors and laymen, known as WARDS (Welfare of Animals used for Research in Drugs and Surgery), raised $20,000 toward construction of the university addition which will provide 40 inside-outside runs for dogs, isolation sections, ventilated rooms for cages, and places for preparation of food and sterilization of equipment.



Top, model research animal quarters to be dedicated July 1 at Georgetown University Medical School. *Bottom*, Father Thomas J. O'Donnell, regent of the medical school, receives WARDS donation from executive committee member, Mrs. Drew Pearson, holding Sandy, a canine heart patient. (*Washington Post* photo.)

This initial effort of WARDS will be followed by a similar project at the George Washington University Medical School, and it is hoped that other animal lovers across the country will form comparable committees to benefit research animals by providing them with adequate space for air and exercise while they are serving mankind. Federal matching funds paid remaining costs of the new building at Georgetown University.

Among organizations actively supporting WARDS are eight kennel clubs, the Alexandria Medical Society, the Medical Society of the District of Columbia, the National Society for Medical Research, dental and veterinary medical groups, several hospital boards, and a citizens' federation. Included among 100 WARDS committee members are 16 physicians, two clergymen, and three U. S. senators.

"The miracles of healing made possible by the use of research animals will multiply as greater attention is given to the health and comfort of our helpless 'stand-ins,'" said a WARDS spokesman. "Many diseases which, a few years ago, were fatal to both dogs and humans, have been conquered by research. Better cared for research dogs mean greater accuracy in scientific findings."

SUGGEST GUIDES FOR SOCIETIES SPONSORING PREPAYMENT PLANS

"Sponsorship of a voluntary prepayment medical benefit plan by a county or state medical association indicates progressive growth of the medical profession's basic position that the welfare of the patient is paramount in the physician-patient relationship." So states a report being submitted later this month to the A. M. A. House of Delegates, recommending adoption of guides for medical societies sponsoring voluntary prepayment medical benefit plans. After much study, the A. M. A. Committee on Prepayment Medical and Hospital Service early last month drafted a set of suggested guides for submission to its parent Council on Medical Service. On May 17, the Council voted approval of the draft in its essential form and offered it to the House for action.

The Council-ratified document states: "The wide acceptance of health insurance makes it mandatory that its effectiveness in meeting patient needs be subject, in all its aspects, to constant appraisal. The dynamic character of the prepayment institution, both in expansion of types of protection and enrollment increases, brings new problems as well as benefits. . . . Plans, prepayment or insurance, to finance the cost of medical care, in themselves influence the quality and quantity of medical care." These suggested guides for society-sponsored prepayment plans—the first of several guides—call for

NORTH CAROLINA

Dr. Gross Honored.—Paul M. Gross, Ph.D., vice-president of Duke University, Durham, and president of the Oak Ridge Institute of Nuclear Studies (Tenn.), will become an Honorary Commander of the Civil Division of the Order of the British Empire, through an appointment by Her Majesty, Queen Elizabeth. The citation will be presented to Dr. Gross by Sir Harold Caccia, British ambassador to the United States, in a ceremony in Washington, D. C., for his "outstanding services to the cause of Anglo-American friendship and understanding." Dr. Gross served from 1953 until 1956 as chairman of the Southern Regional Marshall Scholarship Committee, which awarded scholarships to southern students for study in Britain. He has been a member of the Duke faculty since 1919, and also holds the posts of dean of the university and William Howell Pegram Professor of Chemistry.

PENNSYLVANIA

Personal.—Drs. Domer S. Newill, of Connellsville, D. George Bloom, of Johnstown, and Charles B. Hollis, of Philadelphia, have been appointed to membership on the State Board of Medical Examination and Licensure by Gov. George S. Leader. Drs. Newill and Bloom were appointed to fill vacancies, whereas Dr. Hollis succeeds the late Dr. Raymond S. Leopold, of Philadelphia.——Edmond J. Farris, Ph.D., executive director of the Wistar Institute of Philadelphia, delivered the annual Albert G. Swift Lecture May 1 at the New York State University College of Medicine in Syracuse on "Advances in the Treatment of Sterility."——The Nesquehoning American Legion Auxiliary has presented a citation to Dr. Albert N. Redelin "for outstanding work in the Carbon County Tuberculosis and Public Health Society and other welfare agencies." Dr. Redelin, president of the Carbon County Tuberculosis and Public Health Society since 1951, is the clinician at the State Chest Clinic at Lansford.

WISCONSIN

Dr. Turrell Comes to Milwaukee.—Dr. Eugene S. Turrell, associate professor of psychiatry, University of Colorado School of Medicine, Denver, has been appointed medical director of the Milwaukee Sanitarium Foundation and professor of psychiatry at Marquette University School of Medicine, Milwaukee, effective July 1. Dr. Turrell will devote full time to the sanitarium and the medical school. He will be in direct charge of the medical care program at the sanitarium and will organize residency training programs in psychiatry.

HAWAII

Annual Medical Election.—The results of the May 2 election of the Hawaii Medical Association are: president, Dr. William N. Bergin, Hilo; president-elect, Dr. Toru Nishigaya, Honolulu; secretary, Dr. Raymond C. Yap, Honolulu; and treasurer, Dr. Edward F. Cushnie, Honolulu.

Society News.—The following have been elected officers of the Honolulu Pediatric Society for 1958: president, Dr. Clifford K. Kobayashi; recording secretary, Dr. Robert G. Dimler; and corresponding secretary-treasurer, Dr. Donald F. B. Char.

GENERAL

Award for Essay on Surgery of Trauma.—A prize of $400 is to be given by the American Association for the Surgery of Trauma for the best essay on clinical or laboratory research in the surgery of trauma. Manuscripts, accompanied by the curriculum vitae of the author, must be received by Dr. James K. Stack, 700 N. Michigan Ave., Chicago 11, vice-president of the association, not later than Aug. 15. Contestants must be citizens of the United States or of Canada and be in residency or postgraduate training, or in the formative years of practice or teaching. The author of the winning essay will be invited to read it at the association's annual meeting, to be held at the Drake Hotel, Chicago, Oct. 2-4. The essay will be published in the *American Journal of Surgery*.

Expand Program for Practical Nurses.—Expansion of the program of the National Association for Practical Nurse Education, agency pioneering in the development of schools or practical nursing throughout the country for the past 17 years, has been announced. More than 50,000 members of state associations of practical or vocational nurses will be affected by the doubling of NAPNE's organizational structure to include a new Division of Services to State Associations, beginning June 1. To finance its expanded program, the association has adopted a budget of $200,000 for the coming year. This was made possible through grants totaling $85,000 from various foundations.

Meeting on Tuberculosis in San Francisco.—The 1958 annual meeting of the American Academy of Tuberculosis Physicians will be held June 21 at the Hotel Whitcomb, San Francisco, with Dr. Louis M. Barber, of Stockton, Calif., president of the academy, presiding. Fifteen papers are scheduled for presentation at the two sessions. Guest speaker at the luncheon will be Dr. Robert H. Alway, dean, Stanford University School of Medicine, San Francisco, who will speak on "Physicians for the Future." Dr. Barber will present the presidential address, "Present Trends and Problems in Tuberculosis," preceding the presentation of awards at the luncheon. For information write the American Academy of Tuberculosis Physicians, P. O. Box 7011, Denver 6.

Neurologists Meet in Atlantic City.—The 83rd annual meeting of the American Neurological Association will be held June 16-18 at the Hotel Claridge, Atlantic City, N. J. Dr. Israel S. Wechsler, New York City, will give the presidential address. Forty-two papers are scheduled. Four demonstrations are planned: "Use of Focused Ultrasound in Neurological Research," "Cerebral Defects by the Technique of Transillumination," "Thalamus, Cortex and Visceral Brain in Cerebral Disorders," and "Early Treatment of Ruptured Intracranial Aneurysms." The annual dinner will be held June 17, 7:00 p. m. The American Association of Neuropathologists will hold an evening meeting at the Claridge Hotel June 15 and 16. For information write Dr. Charles Rupp Jr., 133 S. 36th St., Philadelphia 4.

Diabetes Association Meets in San Francisco.—The 18th annual meeting of the American Diabetes Association will be held June 21-22 at the Hotel Mark Hopkins, San Francisco. The program includes 22 scheduled papers. The Banting Memorial Lecture will be given June 21 by Dr. Jerome W. Conn, director, metabolism and research unit, University of Michigan Medical School, Ann Arbor, on e Prediabetic State in Man: Definition, Inter- tion and Implications." At the banquet June , 7:30 p. m., Dr. John A. Reed, president of the association, will present an address, the Lilly award will be presented to Dr. James B. Field, Bethesda, Md., and the Banting Medal will be presented to Dr. Conn. For information write the American Diabetes Association, Inc., 1 E. 45th St., New York 17.

Disabling Illnesses Increase in 1957.—The Metropolitan Life Insurance Company Information Service reports that the incidence of disability lasting eight days or longer was about 17% higher in 1957 than in the previous year, due largely to the wide prevalence of Asian Influenza and other respiratory disorders in the final quarter of the year. Females experienced a much greater increase in frequency of disability than did male personnel. While the rate for men was about two-fifths higher in the last quarter of 1957 than in the corresponding period of the year before, the incidence of disability among women more than doubled. For the year as a whole, the increase was less than 10% for males and about 25% for females. Respiratory diseases ranked first among causes of disability for both women and men. Accidental injuries ranked second for the women and digestive disorders second for the men.

Institute on Medical Teaching in Buffalo.—The University of Buffalo and the Association of American Medical Colleges will present a Summer Institute on Medical Teaching June 16-27 "to provide a limited number of medical instructors with an opportunity to examine in some detail the problems they face in creating effective learning experiences for their students." Included will be presentation of such topics as the appraisal of student performance in clinical and laboratory settings; the use of lecture, laboratory, conference, and other techniques; the nature of the medical student population; and the historical and philosophical background of higher education as it relates to medical education. Institute leaders will include members of the university faculty. For information write Dr. George E. Miller Jr., University of Buffalo School of Medicine, Buffalo 14, N. Y.

Dermatologists Meet in San Francisco.—The 19th annual meeting of the Society for Investigative Dermatology, will be held at The Clift, San Francisco, June 21-22. Of 33 scheduled papers the following include foreign authors:

Tissue Edema—A Stimulus of Connective Tissue Regeneration, Drs. Gustav Asboe-Hansen, Martin Ole Dyrbye, Erik Moltke, and Otto Wegelius, Connective Tissue Research Laboratory, University Institute of Medical Anatomy, Copenhagen, Denmark.

Radiosodium Clearance from the Skin in Certain Cutaneous Circulatory Disorders, Dr. Ernest A. Fairburn, Queen Elizabeth Hospital, Birmingham, England.

The presidential address, "Morphology in Medicine; A Reawakening," will be given by Dr. Walter C. Lobitz Jr., of Hanover, N. H. For information write Dr. Herman Beerman, Secretary-Treasurer, Society for Investigative Dermatology, 255 S. 17th St., Philadelphia 3.

Regional Meeting at San Francisco.—The Northern California and Nevada regional meeting of the American College of Physicians will be held June 18 at the University of California Medical Center auditorium, San Francisco. A program on Fluid and Electrolyte will be presented in the morning with Harold A. Harper, Ph.D., presiding, and a program on Renal Diseases, with Dr. Henry D. Brainerd presiding, will be held in the afternoon. Topics by invited guest speakers include:

Hyponatremic and Hypernatremic States: Osmotic Aspects of Electrolyte Metabolism, Dr. Harper.

Role of Electrolyte in Regulation of Acid Base Equilibrium

–Fundamental Principles and Clinical Application, Dr. Ralph H. Kellogg, Berkeley, Calif.
Effects of Adrenal and Pituitary Hormones on Fluid and Electrolyte Metabolism, Dr. William F. Ganong, Berkeley, Calif.
Chronic Renal Failure, Dr. James Hopper, San Francisco.

Guest speaker at the evening session will be Dr. Dwight L. Wilbur, president of the college, who will present "The Third Person in Medicine." For information write the American College of Physicians, 4200 Pine St., Philadelphia 4.

Cardiovascular Meeting in San Francisco.—The sixth scientific meeting of the International Cardiovascular Society, North American Chapter, will be held June 21 at the Marines' Memorial Theater, San Francisco. A panel discussion, "Surgical Management of Coronary Insufficiency," will be moderated by Dr. Harris B. Shumacker Jr., Indianapolis. Twenty papers are scheduled, including the following with invited guest authors:

Study of Elasticized Dacron as Arterial Prosthesis: Experimental Comparison with Other Plastics, Homologous Arteries and Autogenous Veins, Drs. W. Andrew Dale and Faustino Niguidula, Rochester, N. Y.
Effects of Exposure and Infection of Synthetic Arterial Prostheses, Drs. Robert J. Schramel and Oscar Creech Jr., New Orleans.

The presidential address, "Human Values in Medicine" will be given by Dr. Shumacker at the annual dinner to be held at the Sir Francis Drake Hotel at 6:30 p. m. For information write Dr. Henry Haimovici, Secretary, North American Chapter, International Cardiovascular Society, 105 E. 90th St., New York 28.

Gerontology Awards for Summer Fellowships.—The Inter-University Council of the Institute for Social Gerontology has awarded 36 faculty fellowships for the 1958 Summer Institute in Gerontology. The fellows have been drawn from 36 universities and colleges in 24 states representing every region of the United States. The institute, to be held in August on the campus of the University of Connecticut, will provide intensive training in gerontology, "to increase the number of university and college faculty in the psychological and social sciences prepared to offer instruction and carry on research dealing with the phenomena of aging in American society." The Institute was established last year, with headquarters at the University of Michigan, through a grant from the National Institutes of Health of the U. S. Public Health Service. Sixteen universities are cooperating in the development of its program: California, Chicago, Connecticut, Cornell, Duke, Florida, Illinois, Iowa, Michigan, Minnesota, Pennsylvania State, Pittsburgh, Purdue, Syracuse, Washington (St. Louis), and Wisconsin. Directing the program is Wilma T. Donahue, Ph.D., chairman of the division of gerontology, University of Michigan, Ann Arbor.

World Tour for Four Physicians.—Under sponsorship of the Baptist World Alliance, four physicians chosen on the basis of their "professional competence and their Christian dedication," will leave San Francisco June 27 and visit clinics and hospitals around the world before returning to New York in late September. They will confer with local medical personnel in all areas and offer their services where needed. The team includes Dr. Stanley W. Olson, dean, Baylor University College of Medicine, Houston, Texas; Dr. Robert A. Hingson Jr., professor of anesthesia, Western Reserve University, Cleveland; Dr. John G. P. Cleland, director of the Cleland Clinic, Oregon City, Ore., and Dr. Charles L. Black, a chest surgeon of Shreveport, La. The team will visit mission stations and medical centers in Hawaii, Japan, Korea, and countries of Southern Asia and the Middle East, including Jerusalem and the Gaza Strip; will attend meetings of the Baptist World Alliance Executive Committee in Ruschlikon-Zurich, Switzerland, Aug. 2-8; and will tour mission stations in Africa, including Dr. Albert Schweitzer's Lamberene Hospitals. Invitation for one or more team members to visit local areas should be sent to the Baptist World Alliance, 1628 Sixteenth St., N. W., Washington 9, D. C.

Society News.—The following officers of the American Orthopsychiatric Association have been installed: Dr. Stanislaus A. Szurek, of San Francisco, president; and W. Mason Mathews, Ph.D., Detroit, president-elect. Executive secretary is Marion F. Langer, Ph.D., and headquarters are at 1790 Broadway, New York City.——The following officers of the American Psychosomatic Society took office March 29: Drs. Milton Rosenbaum, New York City, president; and Morton F. Reiser, Washington, D. C., secretary-treasurer. The 16th annual meeting of the society will be held May 2-3, 1959, in Atlantic City.——The following officers were elected for 1958-59 by the American Association for Cleft Palate Rehabilitation: president, Jack Matthews, Ph.D., Pittsburgh; president-elect, Dr. Jacob J. Longacre, Cincinnati; vice-president, Samuel Pruzansky, D.D.S., Chicago; secretary-treasurer, Duane C. Spriestersbach, Ph.D., Iowa City; and editor, Ernest H. Hixon, D.D.S., Iowa City.——Dr. Isidor S. Ravdin, John Rhea Barton Professor of Surgery, University of Pennsylvania School of Medicine, Philadelphia, has been elected president of the American Surgical Association. Other officers include treasurer, Dr. John C. Burch, Nashville, Tenn.; secretary, Dr. William A. Altemeier, Cincinnati; recorder, Dr. John E. Dunphy, Boston; vice-president, Dr. John D. Stewart, Buffalo; and vice-president, Dr. Frederick G. Kergin, Toronto.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	May 17, 1958		May 18, 1957 Total
	Paralytic Type	Total Cases	
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	..	..	..
Middle Atlantic States			
New York	1	1	..
New Jersey	..	1	..
Pennsylvania	..	..	1
East North Central States			
Ohio	..	..	1
Indiana	1	1	..
Illinois	..	1	1
Michigan	..	1	4
Wisconsin	..	..	..
West North Central States			
Minnesota	..	..	..
Iowa	..	..	1
Missouri	..	..	..
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	..	..	..
Kansas	..	..	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	1	1	..
Virginia	..	..	..
West Virginia	1	1	..
North Carolina	..	..	1
uth Carolina	..	..	..
gia	..	..	1
rida	1	4	2
t South Central States			
Kentucky	1	1	..
Tennessee	..	..	1
Alabama	..	..	..
Mississippi	1	1	1
West South Central States			
Arkansas	..	..	5
Louisiana	..	..	1
Oklahoma	..	..	..
Texas	4	5	23
Mountain States			
Montana	..	1	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	1
New Mexico	..	..	1
Arizona	1	3	..
Utah	1	1	..
Nevada	..	1	..
Pacific States			
Washington	..	..	..
Oregon	..	..	..
California	1	2	14
Territories and Possessions			
Alaska	..	..	..
Hawaii	3	3	..
Puerto Rico	..	..	..
Total	17	29	59

Traumatic Surgeons Organize.—An organizational meeting of the newly formed Rocky Mountain Traumatic Surgical Association was held at Aspen, Colo., Feb. 12-16. Officers elected were: Drs. Robert R. Oden, Chicago, president; Alfred C. Buergler, Akron, Ohio, vice-president; and Charles B. Bartell, Long Beach, Calif., secretary-treasurer. It was agreed to have an annual meeting in Aspen, and the dates of the 1959 meeting are tentatively Jan. 25-29. For information write Dr. Charles B. Bartell, 1600 Orange Ave., Long Beach 13, Calif.

CANADA

Annual Medical Meeting in Halifax.—The 91st annual meeting of the Canadian Medical Association will be held June 16-20, with headquarters at the Nova Scotian Hotel, Halifax. Thirteen topics are scheduled for a clinical program in color television, June 16-18. Round-table conferences on the following topics are planned: ear, nose and throat problems in children; recent advances in anesthesia; psychiatry in general practice; recent advances in dermatological therapy; and current obstetrical problems. Papers to be presented at the general sessions are:

Evolution of Infectious Diseases in the Course of History (The Blackader Oration), Rene J. Dubos, Ph.D., New York City.
Problems in Cytodetection of Early Carcinoma of the Cervix, Dr. Malcolm B. Dockerty, Rochester, Minn.
Rheumatic Fever—Prevention and Treatment, Dr. David D. Rutstein, Boston.
Relief of Deafness by Means of the Newer Operations, Dr. William J. McNally, Montreal.
Heart Sounds, Aubrey G. Leatham, M.B., London, England.
Medical Treatment of 1000 Cases of Asthma and Rhinitis, Dr. F. S. Grégoire, Montreal.

For information write the Canadian Medical Association, 150 St. George St., Toronto 5, Ontario, Canada.

LATIN AMERICA

Grant to Argentine Medical School.—To strengthen teaching and research in the basic sciences at the Faculty of Medicine of the University of Cuyo, Argentina, The Rockefeller Foundation has made a two-year grant of $100,000 to the university. Located in Mendoza on the Andean slopes of western Argentina, and founded in 1939, the university is to be housed in a University City to be built on a 155-acre park recently donated by the federal government. The Faculty of Medicine, which ensures limited enrollment and selection of students through rigid entrance requirements, has been provided with a large hospital building on the new campus. The federal government has allocated construction funds and building materials valued at almost $400,000. In the department of physiology studies are being carried out on the physiology of respiration and muscular exercises, on cardiovascular physiology, and on arterial hypertension. Another research program, being developed in the department of histology and embryology, includes work in histophysiology of reproduction, in spermatogenesis in mammals and other vertebrates, and on the pituitary gland. A third area of emphasis in basic research is represented by the recent creation of an Institute of Biology within the Faculty of Medicine, where investigations are being continued on the ecology of amphibia.

FOREIGN

Society for the Study of Metabolism.—At the seventh meeting of the Italian Society for the Study of Metabolism in Milan in March, papers were presented on mucopolysaccharides and mucoproteins. A symposium on the factors of protein anabolism took place on the second day. Prof. Giulio C. Dogliotti (Turin) reported on his results in the treatment of underweight subjects and patients who had protein depletion with 4-chlorotestosterone acetate. The best results were obtained in those with pituitary insufficiency, hypoadrenocorticism, and hyperthyroidism. As a result of its lack of androgenic stimulation, the new steroid reportedly may be found useful in many aspects of human pathology.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written Examination.* Various locations in the United States and Canada, June 18. *Oral Examination.* San Francisco, Sept. 29-Oct. 3, and Phoenix, April 5-10, 1959. The 1959 written examination will be given in various locations in the United States and Canada, July 17. The final date for filing application for the 1959 written examination is six months prior to the examination. There is no filing deadline for oral examinations. Sec., Dr. Curtiss B. Hickcox, 217 Farmington Ave., Hartford 8, Conn.

American Board of Dermatology: *Written. Several Cities,* June 30. *Oral.* Detroit, Oct. 17-19. Final date for filing all applications is April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Written.* Oct. 20, 1958. *Oral.* Philadelphia, April 23-26; San Francisco, June 18-21; Chicago, Oct. 13-16. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: Applications for certification, new and reopened, Part I, and requests for re-examination Part II, are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of application is September 1, 1958. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written,* qualifying test (Part I), January 1959. Final date for filing application is July 1, 1958. *Oral Examinations 1958* (Part II): San Francisco, June 17-21; Chicago, Oct. 17-22. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago, Jan. 21-23, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 6-10. Final date for filing application was April 30. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Chicago, Oct. 30-Nov. 1. Final date for filing application is Sept. 30. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Oral.* Cincinnati, June 13-15; Chicago, Oct. 24-26 and New York, Dec. 5-7. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Oral and Written.* Peoria, Ill., June 20-21. Final date for filing application was Feb. 1. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Chicago, Oct. 9-11. Final date for receipt of case reports is July 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

American Board of Proctology: *Oral and Written, Parts I and II.* September 1958. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Regular Examination in Radiology.* Washington, D. C., Dec. 8-12. Final date for filing application is July 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Oral (Part II).* Los Angeles, June 16-17; Portland, June 20-21. Written examinations (Part I) will be held at various centers in the United States, Canada, Hawaii, Puerto Rico, and certain military centers abroad on December 3. The date of the Fall examination in *Part I* has been changed from the last Wednesday of October as announced in its current Booklet of Information to December 3, 1958. Thereafter, examinations in Part I will be held once annually, on the first Wednesday of December. The closing date for filing applications will be August 1. *Part II.* Baltimore, March 10-11. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: The fall written examination will be given in September 1958 and closing date for registration is July 1. Registration for the fall oral examination closes July 1.

American Board of Urology: *Written Examination.* Twenty-five cities throughout the country, Dec. 5. The oral will be given in Chicago in February 1959. Sec., Dr. William Niles, Wishard, Jr., 30 Westwood Road, Minneapolis 26.

Corbett, Elizabeth Louise Ufford, San Jose, Calif.; University of Kansas School of Medicine, Kansas City, Kan., 1943; specialist certified by the American Board of Pathology; an associate member of the American Medical Association; interned at the Albany (N. Y.) Hospital; served a residency in pathology at Grasslands Hospital in Valhalla, N. Y., and the Kansas Medical Center in Kansas City, Kan.; served on the staff of the San Jose Hospital; died March 23, aged 41, of leukemia.

Covert, Jay Byington, Geneva, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1902; an associate member of the American Medical Association; associated with the Geneva General Hospital; died March 25, aged 82, of arteriosclerosis and hypertension.

Crow, Will Frame, Moundsville, W. Va.; Eclectic Medical Institute, Cincinnati, 1894; veteran of World War I; formerly member of the legislature, serving as a member of the House of Delegates from Marshall County; died in Sistersville March 26, aged 92.

Cummings, Michael Penn, Reidsville, N. C.; Jefferson Medical College of Philadelphia, 1911; past-president of the Rockingham County Medical Society; for many years county coroner and city health officer; served as mayor; on the staff of the Annie Penn Memorial Hospital; died March 30, aged 71, of a heart attack.

Devere, Frederick Hewitt ⊕ Cranston, R. I.; University of Vermont College of Medicine, Burlington, 1898; died in the Roger Williams General ospital, Providence, March 29, aged 83, of pul- y edema.

C. Harold ⊕ Fulton, Mo.; Northwestern ersity Medical School, Chicago, 1939; veteran World War II; a member of the staff of State Hospital number 1; died in Boone County Hospital, Columbia, March 31, aged 46, as the result of a fall.

Donald, E. Wendell, Kansas City, Kan.; University of Oklahoma School of Medicine, Oklahoma City, 1942; member of the Kansas Medical Society and the American Academy of General Practice; veteran of World War II; formerly practiced medicine in Caldwell, where he was a member of the school board; on the staffs of the Veterans Administration Hospital in Kansas City, Mo., and the University of Kansas Medical Center; died in Prairie Village March 1, aged 43, of carcinomatosis.

Dutcher, Willis Woodford, Los Angeles; Albany (N. Y.) Medical College, 1906; died March 25, aged 80.

Fidler, Charles ⊕ Milwaukee; Rush Medical College, Chicago, 1906; formerly on the faculty of the Marquette University School of Medicine; fellow of the American College of Surgeons; past-president of the State Medical Society of Wisconsin; served as secretary and president of the Medical Society of Milwaukee County; veteran of World War I; an honorary member of the staff of Milwaukee Children's Hospital; associated with Columbia Hospital and St. Mary's Hospital, where he died March 27, aged 77, of periarteritis nodosa.

Fox, Francis Harry, Las Vegas, Nev.; Jefferson Medical College of Philadelphia, 1902; died March 20, aged 77, of cerebral hemorrhage.

Frazin, Nathaniel Daniel ⊕ Silver City, N. M.; Northwestern University Medical School, Chicago, 1911; died April 10, aged 68.

Gaetane, Joseph Anthony ⊕ Flushing, N. Y.; Boston University School of Medicine, 1937; certified by the National Board of Medical Examiners; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; veteran of World War II; president of the Queens Gynecological Society; associated with the Queens General and Mary Immaculate hospitals in Jamaica, and the Flushing (N. Y.) Hospital, where he died April 1, aged 47, of carcinoma of the rectosigmoid.

Garrett, Frank Bernard, Rockingham, N. C.; North Carolina Medical College, Charlotte, 1912; member of the Medical Society of the State of North Carolina; died in the Duke Hospital, Durham, March 27, aged 67, of uremia.

Hamilton, E. Mendel, Belington, W. Va.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1897; an associate member of the American Medical Association; served as city health officer; died March 22, aged 86, of chronic myocarditis.

Harbaugh, Ross Wallace, San Francisco; Stanford University School of Medicine, San Francisco, 1913; an associate member of the American Medical Association; died April 2, aged 73, of injuries received in an automobile accident.

Harris, Harry Gustavus, Dayton, Ohio; New York Homeopathic Medical College and Flower Hospital, New York City, 1912; died March 25, aged 80, of arteriosclerotic heart disease.

Harshberger, Joseph Walter, Fayetteville, Pa.; Chicago College of Medicine and Surgery, 1911; veteran of World War I; died in the Philadelphia Freemason's Memorial Hospital, Elizabethtown, March 21, aged 72, of cerebral hemorrhage.

Higgins, Robert Frank ⊕ Tuskegee, Ala.; University of Tennessee College of Medicine, Memphis, 1931; veteran of World War II; died in Fort Lauderdale Beach, Fla., March 27, aged 56.

Hord, Benjamin A. ⊕ Richmond, Va.; Medical College of Virginia, Richmond, 1898; associated with the Stuart Circle Hospital; died March 23, aged 80, of uremia.

Illsley, Wilbur Wallace, Fullerton, Calif.; Kansas City (Mo.) University of Physicians and Surgeons, 1924; veteran of World War I; died in St. Joseph Hospital, Santa Ana, March 30, aged 67, of heart disease.

Jacobson, Clara ⊕ Chicago; Rush Medical College, Chicago, 1913; member of the American Trudeau Society; for many years on the staff of the South Shore Hospital; died April 13, aged 70, of acute coronary occlusion.

Jones, Thomas Edward, Washington, D. C.; Howard University College of Medicine, Washington, 1912; formerly on the faculty of his alma mater; served in France during World War I and won the Distinguished Service Cross for gallantry in action; also held the French Croix de Guerre for extraordinary heroism in action near Binarville, France; for many years associated with the Freedman's Hospital; died April 4, aged 77, of coronary thrombosis.

Kohlenbach, Stephen ⊕ Columbia, Ill.; St. Louis College of Physicians and Surgeons, 1902; died in St. Mary's Hospital, East St. Louis, March 13, aged 85.

Kraft, Adolph ⊕ Chicago; University of Illinois College of Medicine, Chicago, 1922; fellow of the International College of Surgeons and the American College of Surgeons; associated with Oak Park (Ill.) Hospital, Belmont and Loretto hospitals, and St. Anne's Hospital, where he died April 15, aged 62, of acute myocardial infarction.

Kuhn, Hugh Alva Ross ⊕ Hammond, Ind., born Nov. 16, 1895; University of Cincinnati College of Medicine, 1921; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology, Indiana Academy of Otolaryngology, of which he was past-president, American Laryngological, Rhinological and Otological Society, American Society of Ophthalmic and Otolaryngologic Allergy, of which he was past-president and vice-president, and the American College of Allergists, serving as regent, and in 1957 vice-president; fellow of the International College of Surgeons; secretary of the Section on Laryngology, Otology and Rhinology, American Medical Association from 1953 to 1958; member of the board of directors of the Hansel Foundation; veteran of World War I; medical superintendent of the Kuhn Clinic Hospital; consultant on the staff, South Chicago Community Hospital in Chicago; staff member of St. Margaret Hospital in Hammond, St. Catherine's Hospital, East Chicago, and Our Lady of Mercy Hospital in Dyer; in 1957 received the doctor of science degree from Muskingum College in New Concord, Ohio; died in Chicago April 17, aged 62, of coronary occlusion.

Lamberth, James Vann ⊕ Pineville, La.; Louisiana State University School of Medicine, New Orleans, 1953; interned at T. E. Schumpert Memorial Sanitarium in Shreveport; later practiced in De Quincy; associated with the Central Louisiana State Hospital; died March 23, aged 37, of asphyxiation as the result of a fire in his home.

Latimer, James Brockington ⊕ Lieut., U. S. Navy, retired, Anderson, S. C.; Medical College of South Carolina, Charleston, 1917; entered the U. S. Navy in 1917 and retired Sept. 19, 1921; veteran of World War I; associated with Anderson Memorial Hospital, where he died April 1, aged 66, of carcinoma of the lung with metastases.

Lawson, Henry Carnie ⊕ Fall River, Mass.; Cornell University Medical College, New York City, 1932; certified by the National Board of Medical Examiners; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; consultant, St. Anne's Hospital; chief of obstetrics and gynecology service, Union Hospital, where he died March 25, aged 51, of acute myocardial infarction and hypertension.

Levin, Harris ⊕ Senior Surgeon, U. S. Public Health Service Reserve, Philadelphia; Temple University School of Medicine, Philadelphia, 1947; service member of the American Medical Association; specialist certified by the American Board of Pediatrics; veteran of the Korean War; associated with the Graduate Hospital of the University of Pennsylvania and Albert Einstein Medical Center, Northern Division; certified by the National Board of Medical Examiners; died April 8, aged 35.

Lewis, George Willard, Pierpont, Ohio; Western Pennsylvania Medical College, Pittsburgh, 1895; veteran of World War I; associated with the Brown Memorial Hospital in Conneaut, where he died March 25, aged 87.

Little, Edwin Gray ⊕ Gadsden, Ala.; Birmingham Medical College, 1905; associated with Holy Name of Jesus Hospital and Baptist Memorial Hospital; died March 23, aged 78, of bronchopneumonia.

McClure, Daniel Vincent, Buffalo; Niagara University Medical Department, Buffalo, 1894; past-president of the Medical Society of the County of Erie; died March 6, aged 84.

McCreery, Albert Hill, Chapel Hill, N. C.; University of Pittsburgh School of Medicine, 1913; an associate member of the American Medical Association; formerly practiced medicine in Pittsburgh, where he was associated with the Shadyside Hospital; died in the North Carolina Memorial Hospital March 23, aged 67.

McDonald, John ⊕ San Francisco; College of Physicians and Surgeons of San Francisco, 1921; veteran of World War I; died in Crawfordsville, Ind., March 28, aged 66.

McDonald, Robert Clarence ⊕ Brigadier General, U. S. Army, retired, Washington, D. C.; born in Bells, Tenn., Feb. 18, 1881; Tulane University School of Medicine, New Orleans, 1909; service member of the American Medical Association; fellow of the American College of Surgeons; entered the medical corps of the regular Army in February, 1911; saw duty on the Mexican Border; served in France during World War I; awarded the Legion of Merit for exceptionally meritorious conduct in the performance of outstanding services as surgeon, Fourth Service Command; retired Feb. 28, 1945; died in the Walter Reed Army Hospital March 17, aged 76, of arteriosclerotic heart disease.

McDowell, Orrin Clark ⊕ Orrville, Ohio; Ohio State University College of Medicine, Columbus, 1917; veteran of World War I; died March 28, aged 64, of cerebral embolism and bacterial endocarditis.

Makowski, Stanley Joseph ⊕ Glen Cove, N. Y.; Rush Medical College, Chicago, 1931; certified by the National Board of Medical Examiners; fellow of the International College of Surgeons and the American College of Surgeons; associated with Meadow Brook Hospital in Hempstead, St. Charles pital in Port Jefferson, and the Community spital, where he died April 4, aged 54, of cereral thrombosis.

Miller, James Preston, DeLand, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1898; University of Nashville (Tenn.) Medical Department, 1900; died March 10, aged 82.

Morrow, Frank M., Leavenworth, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1905; died in the University of Kansas Medical Center, Kansas City, March 13, aged 78, of a cerebral vascular accident.

Neef, Frederick Emil, Middlebury, Vt.; born July 11, 1872; Columbia University College of Physicians and Surgeons, New York City, 1904; fellow of the American College of Surgeons; formerly practiced medicine in New York City, where he was on the faculty of the Fordham University School of Medicine, and on the staffs of Lincoln, St. Elizabeth's, St. Francis, Lenox Hill and Misericordia hospitals; served on the staff of the Rockaway Beach (N. Y.) Hospital; author of a textbook of "Surgical Nursing"; died in the Porter Memorial Hospital March 24, aged 85, of arteriosclerosis.

O'Connell, Thomas Andrew, Brookline, Mass.; College of Physicians and Surgeons, Boston, 1937; died March 11, aged 61.

O'Hara, John Gerald ⊕ Woodland, Calif.; St. Louis University School of Medicine, 1936; member of the American Academy of General Practice; past-president of the Yolo County Medical Society; major in the medical corps of the U. S. Army from 1953 to 1955, serving in Korea and Japan; served as part-time health officer of Yolo County; associated with the Mercy and Sutter hospitals in Sacramento, and Yolo General Hospital; died March 20, aged 46, of lung cancer.

Polk, Joseph Feaston, Slidell, La.; Memphis (Tenn.) Medical College, 1900; died March 22, aged 82.

Powell, Robert Joshua ⊕ Atlantic City, N. J.; Howard University College of Medicine, Washington, D. C., 1914; past-president of the Medical Society of New Jersey; died March 24, aged 71, of cerebral embolism.

Power, George Aloysius, Worcester, Mass.; Harvard Medical School, Boston, 1909; member of the Massachusetts Medical Society; served as city physician and as a member of the board of education; died in St. Vincent Hospital March 22, aged 74, of arteriosclerotic heart disease.

Rogers, Henry William, San Rafael, Calif.; University and Bellevue Hospital Medical College, New York City, 1919; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; veteran of World War I; served as chief psychiatrist at the California State Prison in San Quentin; chief psychiatrist at the Department of Corrections Reception Guidance Center in Vacaville; died in the San Rafael General Hospital March 28, aged 66, of cerebral hemorrhage.

Roth, Julius Andrew ⊕ Delray Beach, Fla.; St. Louis University School of Medicine, 1930; veteran of World War II; associated with Good Samaritan and St. Mary's hospitals in West Palm Beach; chief of obstetrics and gynecology at Bethesda Hospital; died March 19, aged 51, of coronary thrombosis.

Schell, Charles Peter ⊕ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; member of the American Academy of General Practice; served on the staff of St. Mary of Nazareth Hospital; died April 10, aged 85, of a cerebral vascular accident.

Schneller, Edwin Jacob ⊕ Racine, Wis.; Rush Medical College, Chicago, 1925; member of the American Academy of General Practice; past-president of the Racine County Medical Society; veteran of World War I; associated with St. Luke's Hospital, where he died March 27, aged 64, of acute coronary thrombosis.

Schroeder, Frank Nicholas ⊕ Ryan, Iowa; St. Louis College of Physicians and Surgeons, 1905; died in the Mercy Hospital, Cedar Rapids, March 24, aged 80, of coronary occlusion.

Scifres, Zach McNorman, Louisville, Ky.; Indiana University School of Medicine, Indianapolis, 1915; died in the Norton Memorial Infirmary March 8, aged 77.

Shaw, Francis Clark, Dannemora, N. Y.; University of Vermont College of Medicine, Burlington, 1920; member of the American Psychiatric Association; director of the Dannemora State Hospital; served on the staffs of Matteawan State Hospital in Beacon, and Lawrence State Hospital in Ogdensburg; died in the Montreal General Hospital, Montreal, Que., Canada, April 6, aged 61.

Slanec, Charles George ⊕ Chicago; Chicago Medical School, 1922; veteran of World War I; died April 10, aged 66, of acute coronary occlusion.

Slopanskey, Frank Robert, Salt Lake City; Denver and Gross College of Medicine, 1905; specialist certified by the American Board of Ophthalmology; fellow of the American College of Surgeons; formerly practiced medicine in Helper, Utah, where he was mayor, and vice-president of the Helper State Bank; a staff member of St. Mark's Hospital; died March 29, aged 78.

Stanard, Delbert Coshow ⊕ Eugene, Ore.; University of Oregon Medical School, Portland, 1921; past-president of the Lane County Medical Society; veteran of World Wars I and II; died in the Sacred Heart General Hospital March 27, aged 67, of cirrhosis of the liver.

Stark, Leander William, Long Beach, Calif.; College of Physicians and Surgeons, Los Angeles, 1919; an associate member of the American Medical Association; died March 25, aged 66, of acute coronary thrombosis.

Suwalsky, Adelbert L. ⊕ Leavenworth, Kan.; Medico-Chirurgical College of Kansas City, Mo., 1901; served as city physician and county health officer; associated with Cushing Memorial Hospital and St. John's Hospital, where he died March 27, aged 78, of gangrenous cholecystitis, coronary sclerosis, and pulmonary edema.

Tran, Irving ⊕ Brooklyn; Cornell University Medical College, New York City, 1909; fellow of the American College of Surgeons; associated with the Jewish Hospital; died April 3, aged 70, of a heart attack.

Vest, Samuel Alexander Jr., Charlottesville, Va.: born in Haw River, N. C., Jan. 21, 1905; Johns Hopkins University School of Medicine, Baltimore, 1930; specialist certified by the American Board of Urology; professor and chairman of the department of urology at the University of Virginia Department of Medicine; formerly associate in urology at Johns Hopkins University School of Medicine and on the staff of the Johns Hopkins Hospital in Baltimore; served as vice-president of the Virginia Urological Society; member of the American Association of Genito-Urinary Surgeons and the American Urological Association; fellow of the American College of Surgeons; on the staff of the University of Virginia Hospital, where he died April 6, aged 53, of acute myocardial infarction.

Webb, Lewis Monson ⊕ St. Louis; St. Louis University School of Medicine, 1925; associated with Deaconess and Bethesda hospitals; died in Fort Lauderdale, Fla., April 2, aged 61, of coronary occlusion.

Weinstein, Samuel ⊕ Richmond, Va.; Medical College of Virginia, Richmond, 1925; veteran of World War I; associated with the Stuart Circle Hospital and the Retreat for the Sick; died April 3, aged 61, of coronary thrombosis.

Weir, Claud Hill ⊕ Seattle; Columbia University College of Physicians and Surgeons, New York City, 1904; specialist certified by the American Board of Otolaryngology; died in the Fairfax Sanitarium in Juanita March 8, aged 80, of carcinoma of the prostate.

Whitacre, Floyd Stanley ⊕ San Antonio, Texas: St. Louis College of Physicians and Surgeons, 1909; for many years a director of the Abilene (Texas) Christian College; died March 25, aged 75, of basilar cerebral artery syndrome, arteriosclerosis, and Laennec's hepatic cirrhosis.

Whitmire, William Lincoln ⊕ Sumner, Iowa; Rush Medical College, Chicago, 1890; died in the Community Memorial Hospital March 25, aged 93, of arteriosclerosis.

Wilson, Franklin Samuel ⊕ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1911; assistant professor of medicine emeritus at his alma mater; past-president of the University of Illinois Alumni Association; for many years medical examiner for the Juvenile Home; served with the Cook County Public Welfare Department; associated with the Garfield Park Community Hospital, where he died April 10, aged 85, of carcinoma of the prostate with metastasis.

FOREIGN LETTERS

AUSTRIA

Deafness in Children.—At the meeting of the Society of Physicians in Vienna on April 11, Dr. G. Koenig said that all children who do not react to sound, do not copy speech, or do not speak articulately from the time they are 2 years old should be examined to find the cause. A fairly accurate audiogram can be made for children age 2, but better results are obtained after they reach the age of 3. If a hearing defect is discovered the child should be placed in a special kindergarten where articulation exercises are started. Later systematic hearing training is practiced. As soon as the child reacts to hearing impressions, a hearing aid is provided. The child soon learns to handle the apparatus under proper guidance, but the true value of the hearing aid to the child can be determined only after 6 months of use. Even in children with no residual hearing but with normal intelligence a primitive phonetic communication may be achieved.

Blockage of Ovulation.—At the same meeting Drs. G. Schubert and F. X. Wohlzogen said that ovarian follicles just before they burst contain a substance which splits up the mucopolysaccharides of the liquor folliculi. This splitting and the resultant increase of the osmotic pressure is the eliciting cause of ovulation. Hyaluronidase splits mucopolysaccharides of the hyaluronic acid and chondroitic [illegible]onic acid type, both of which occur in the follicle. It was therefore important to find out whether hyaluronidase blocking agents would also inhibit the splitting of the mucopolysaccharides in the ovarian follicle, thus blocking ovulation. Adult rabbits were given 250 international units of chorionic gonadotropin intravenously to elicit ovulation. Germanin was given intravenously as a hyaluronidase blocking agent, partly simultaneously and partly after the injection of chorionic gonadotropin. The ovaries were removed 15, 24, and 48 hours after the administration of the gonadotropin and were examined macroscopically and histologically. Pretreatment with Germanin alone had no effect on ovulation, but when Germanin was given in such a way that a high level was present at the time of the expected ovulation, the latter was blocked. Thus blocking of ovulation was achieved in a different way than by blocking of the luteinizing hormone of the anterior lobe of the hypophysis by progesterone or inactivation of gonadotropin by antihormones or vegetable extracts. It is essential that neither the gonadotropic function of the anterior lobe of hypophysis nor the hormonal function of the ovary be impaired by the blocking agent.

Liver Biopsy.—At the meeting of the Society of Physicians in Vienna on April 18, Dr. Thaler reported on a new method of liver biopsy that shows one definite advantage over the method previously used, namely that of being performed without the stylet. A series of 170 such biopsies have been performed without any untoward effects. The results were excellent. Complaints after puncture were rare and usually insignificant. Thus the new technique seems to be the method of choice for needle biopsies.

Subdural Hematoma.—At the same meeting Drs. H. Reisner and E. Scherzer reported on 17 patients with subdural hematoma who were referred to the apoplexy ward of a mental hospital with a diagnosis of cerebral accident. Of the 16 patients who were operated on, 13 were cured and 3 died. It was pointed out that subdural hematoma may be present in patients with a diagnosis of cerebral accident in whom neurological symptoms are progressive. In such patients cerebral angiography should be performed.

BRAZIL

Congress of History of Medicine.—At Rio de Janeiro in April under the honorary chairmanship of Dr. Juscelino Kubitschek, President of Brazil and the only chief of state of the Americas who is a physician, the First Pan American Congress of History of Medicine and the third annual meeting of the Brazilian Institute of Medicine was held. The occasion was used to found the Pan American Academy of History of Medicine and to inaugurate, at the National Library, a bibliographic exposition of history of medicine.

Control of Trachoma.—The Ministry of Health issued a report on the campaign begun in 1957 to eradicate trachoma, which, according to the best estimates, afflicts about a million people, or 1.6% of the total population, mostly in rural areas. The work, performed by teams of physicians and nurses of the Division of Rural Hygiene began in two counties in the state of Ceará, where more than 30,000 patients were cured last year. To avoid personal contact between trachomatous patients and healthy persons, the treatment was brought

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The items in these letters are contributed by regular correspondents in the various foreign countries.

to the patient's home. A total of 125,000 houses were visited, and 230,000 persons were treated, for whom 12 million sulfonamide tablets and 363,000 tubes of antibiotics were furnished. The eradication of the disease is expected to be completed within a few years.

The Spermogram.—The idea that azoospermia is the only factor to be considered for the diagnosis of sterility in men has been abandoned, and a complete study, macroscopic and microscopic, of the semen is now deemed necessary. Dr. M. L. Antunes (*O Hospital* 53:383, 1958) reported the results of the examination of the semen of 100 husbands of pregnant women. The volume of the ejaculate varied between 1.5 and 7 cc. (average 3.1). The number of spermatozoa per cubic centimeter varied between 12 million and 214 million (average 80 million). The total number of sperms per ejaculate varied between 25 million and 600 million (average 257 million). The motility of the sperms was between 41 and 90% (average 73%). The vitality of the sperms, expressed by the number still alive 24 hours after the ejaculation, was between 6 and 30% (average 18.2%). The morphology of the sperms, considered one of the best criteria of fertility, was measured in terms of percentage of abnormal forms; 95% of the ejaculates showed abnormal forms in only 6 to 15% of the sperms. The author believes that the abnormal forms should not exceed 20%. Leukocytes were present in small number in 33% of the specimens, rare in 41%, and numerous in 26%. In four specimens the presence of mucus was observed, but no significance was attached to this finding. The presence of Bottcher's spermatic crystals, in examinations made 24 hours after the ejaculation, was noted in 15% of the specimens. Amylaceous corpuscles from the prostate were observed in only one specimen. These bodies are considered as an indication of exhaustion, although the patient claimed a complete abstinence of five days, as recommended by the laboratory.

COSTA RICA

Meeting of Central American Ministers of Health.—At the third meeting of Central American Ministers of Health held in San Jose, Costa Rica, in March, the four main points included in the agenda were as follows: 1. Coordination of the preventive medicine programs for all Central America. Isolated efforts to carry out good preventive programs, if properly coordinated, should give much more satisfactory results. 2. Creation of a Central American Institute of Intravenous Solutions and Vaccines. All Central American countries are spending vast sums for products that could be manufactured locally at a lower cost. 3. Facilities for personnel training. A reasonable number of institutions in this area have qualified technicians who could teach students from neighboring countries. This should relieve the shortage of qualified personnel and the difficulties (language and cost) of training all of them in the United States. 4. Creation of a Mental Health Institute. This would provide ample space for research as well as training in a field in which little advance has as yet been made in Central America.

FRANCE

Intramedullar Transfusions in Newborn.—Since 1945 Salvatore Folena (*Presse Méd.* 66:641, 1958) has used a method of transfusion that is particularly useful in the newborn and the infant. The method consists in utilizing the transosseous and particularly the intrailiac route. The author concluded that the intrailiac could be substituted for the intravenous route when the approach to the veins appeared difficult, which was usual in the newborn. Furthermore the intrailiac route makes it possible to perform a direct transfusion (from the donor's vein to the bone marrow in the infant) and to avoid or reduce shock, as the injected fluid filters through the bone marrow before reaching the venous system. The ilium has a great absorptive capacity, behaving somewhat like a vast lacunar system communicating with the venous system.

Labyrinthine Vertigo.—J. Cellice and co-workers (*Presse Méd.* 66:592, 1958) used ethanolamine acetyl leucinate (7452 RP) in the form of a 10% acid solution in the treatment of labyrinthine vertigo. This solution, which provokes neither local nor general secondary reactions, was injected intramuscularly or intravenously in doses of 0.5 to 1.0 Gm. of the active principle daily, for periods of from 10 to 15 days. In a series of 31 patients with vertigo due to various causes the authors obtained satisfactory results in 18. The best results were noted in patients with aural vertigo (success in 11 of 13 patients). The drug does not seem to lose its effectiveness and was efficacious against recurrences. On the other hand no improvement could be obtained with it in most patients with auditory hallucinations.

Cytochrome C as Metabolic Inhibitor.—H. Laborit and co-workers (*Presse. Med.* 66:597, 1958) in a previous study demonstrated certain virtues of cytochrome C in animals. As a consequence of this study a solution containing a potassium salt of cytochrome C was prepared for use in man. This study led to the same conclusion: the solution of cytochrome C inhibited the velocity of cellular metabolism. It is, therefore, one of the rare agents capable of reducing metabolism without seriously disturbing respiration.

GERMANY

Genetic Aspects of the Neuroses.—P. E. Becker (*Dtsch. med. Wchnschr.* 83:612, 1958) stated that there has been a genuine increase in the incidence of neuroses in the last few decades; 40% of patients in a neurological practice had functional disorders, most of them neuroses. Factors predisposing to neurosis are acquired during early childhood; the mother plays the decisive role. An infantile emotional pattern and immaturity of the mother may initiate neurotic development. Abnormal irritability, emotional lability, and overprotectiveness may work in the same direction. Because such maternal emotional patterns are often in part genetically determined, the child's emotional structure may be similar. Such qualities as basic mood, sensitiveness, and initiative are largely genetically determined. It has also been shown that the actual neurosis is not inherited. Apart from the more general inherited neurotic disposition, genetic factors apparently play a decisive role in certain forms of neurosis. Thus studies of twins indicated a genetic factor in some cases of homosexuality. In addition, there is an acquired form of homosexuality. Parallel results were obtained in a study of enuresis (by Hallgren). In some cases there was a definite hereditary component. In some forms of addiction and organ neuroses a similar situation may exist.

Postnephritic Hypertension.—O. H. Arnold and K. D. Bock (*Dtsch. med. Wchnschr.* 83:711, 1958) reported a series of 14 patients, many of whom were followed for several years, after the acute ase of glomerulonephritis. In these patients the ary signs of nephritis regressed completely, ile arterial hypertension, indistinguishable from essential hypertension, became progressively more prominent. There was no evidence of abnormal renal function, as measured by the ability to concentrate and the absence of retention, of urea, for example, but para-aminohippuric acid and inulin clearances were normal in seven patients and abnormal in the remaining seven. Although there was in these patients no histological evidence that the renal disease had been cured, the clinical findings, characterized by the absence of all abnormalities in half of them, suggested that the persistent arterial hypertension should be considered a postnephritic hypertension. It is possible that in those patients in whom there was an abnormality in the clearance tests healing had occurred with residual defects. On the basis of results reported in the experimental reproduction of hypertension, a hypothesis is suggested for the pathogenesis of hypertension in the course of chronic glomerulonephritis.

Renal Involvement in Macroglobulinemia.—W. Schrade and co-workers (*Dtsch. med. Wchnschr.* 83:718, 1958) demonstrated small amounts of protein in three patients with macroglobulinemia, using the method of Bohler and Fischer, although sulfosalicylic acid had given negative results. Paper electrophoresis of the urine showed in addition to the albumin and ordinary globulin a prominent fraction which had the same migration velocity as the serum macroglobulin. Ultracentrifuge examinations in two cases showed that the various urinary protein fractions did not have a sedimentation constant greater than that of albumin. In a fourth case of macroglobulinemia, which clinically showed severe nephrotic syndrome and histologically gave evidence of advanced renal amyloidosis, abnormal proteins in addition to large amounts of normal proteins were probably present. The results indicated that as in multiple myeloma so also in macroglobulinemia there is a paraproteinuria; but in macroglobulinemia it is not marked enough to cause nephrosis. This is the reason why renal involvement is usually not a feature of macroglobulinemia, but in this condition, too, renal abnormalities may occur if there is deposition of amyloid in the kidneys.

JAPAN

Diphtheria.—The incidence of diphtheria has been increasing steadily. In 1953 there were 8,381 cases and 639 deaths. In 1956 there were 18,294 cases and 853 deaths. Heretofore it has been the practice to give diphtheria toxoid to the infants between 6 and 12 months old, but it has become apparent that the first immunizing dose should be given at about 3 months, when the immunity transferred from the mother is known to have disappeared. A booster injection is given at the age of about 1 year. A combined diphtheria toxoid and pertussis vaccine is used.

Infant Mortality.—In an effort to reduce the heavy death rate in infants better provisions are being made for the care of those born prematurely. Each year about 110,000, or 6.6%, of live births were premature. Of this number 22,000 babies died in their first year. To combat this situation (1) premature births must now be reported, (2) if the home conditions warrant it, the mother may keep the baby at home, being assisted by the visiting nurse and the midwife (incubators are supplied if needed), and (3) if the home conditions are inadequate the baby is removed to a hospital, at government expense if necessary.

Penicillin Shock.—A 45-year-old man was admitted with old extensive burn scars on the flexor surface of his left knee, with keloid changes in spots. He had no subjective symptoms. A biopsy specimen of the scar was taken and the incision treated with penicillin solution. Shortly thereafter the patient showed signs of shock. He was given repeated blood and plasma transfusions and showed a temporary response, with momentary return of consciousness, only to sink into coma and die on the following day. It was later learned that the patient had had a similar but less severe reaction after taking penicillin several years ago.

Contraception.—Because of severe overcrowding the government about seven years ago sanctioned contraception and even the termination of pregnancy, in certain cases. The case fatality rate following interruption of pregnancy has been less than one per thousand, but morbidity rates are high, the commonest complications being hemorrhage, fever, and headaches. The number of patients so treated, according to the government records, are about a million annually, but half as many more are probably accounted for by private surgery. There is now a definite trend to discourage the interruption of pregnancy and to urge contraceptive measures. This requires educating the mothers by home instructions and group teachings. In this program midwives assist the social workers. In urban areas there has already been a 35% reduction in the birth rate. A similar change is expected in rural districts.

PERU

New Medical Schools.—Exactly 102 years after the creation of the Faculty of Medicine of San Fernando of Lima, attached to the National University of San Marcos, two new medical schools were opened in Peru, one in Arequipa and the other in Trujillo. The Faculty of Medicine of the National University of San Agustin of Arequipa will admit not over 50 new students each year, all of them from southern Peru. This year only 42 applicants were found eligible. One of the best features of this new school is the loan of money to students who would otherwise be unable to attend.

Cancer of Uterine Cervix.—Dr. Mariano Bedoya Hevia, (*Ginecologia y Obstetricia*, vol. 3, Dec., 1957) reported a series of 52 patients with in situ or invasive cancer of the uterine cervix. He stated that total hysterectomy plus resection of one-third of both the vagina and parametrium, with or without bilateral oophorectomy, is the treatment of choice for stage 0 of epidermoid carcinoma or carcinoma in situ. The procedure selected in each case, however, must take into account the patient's age, parity, wish to have children, and presence or absence of associated genital lesions. In stage 1 of the invasive type of cancer, the therapeutic approach depends basically on the signs of sensitization response. Whether surgery or radiation is to be used rests on the results of this test. If operation is indicated, radical total hysterectomy plus lymph node resection should be performed. Irradiation is the method of choice for stage 2, except in patients showing a definitely poor radiation response. When the number of cells in vaginal smears displaying cytoplasmic vacuolization, nuclear changes, enlargement of both cell and nucleus, and multiple nuclei exceeds 60%, the response to radiation is regarded as poor. Radical hysterectomy with lymph node dissection is indicated for this type of patient. In stages 3 and 4 radiation continues to be the most effective treatment for most patients. Recurrences following this treatment call for pelvic exenteration. In carcinoma of the cervical stump operation is the best treatment unless definite contraindications exist. In pregnancy the management of cervical cancer depends on the viability of the fetus and the stage of development of the tumor.

Dehydration in Infants.—Dr. G. Morey and coworkers (*Revista del Hospital del Nino*, vol. 18, Dec. 1957) studied acute dehydration in 375 hospitalized children whose ages ranged from 0 to 3 months in 41 (10.94%), 3 to 6 months in 86 (22.94%), 6 to 9 months in 72 (19.21%), 9 to 12 months in 87 (23.20%), and 1 to 3 years in the remaining 89 patients (23.71%). All had a history of vomiting and diarrhea; 250 (66.67%) showed on admission severe involvement of the nervous system manifested by notable impairment of the sensorium; 42 (11.72%), abdominal distension; 35 (9.33%), muscular hypotonia; 32 (8.52%), generalized edema; and 17 (4.52%), marked restlessness. Only 107 children (28.53%) were found to be lucid on admission. Most patients (82.1%) were febrile, and 216 children (62.56%) were in shock. On admission, the body weight, as compared to the ideal, showed a deficit of 0% in 19 (5.1%), of from 1 to 25% in 100 (26.6%), of from 25.1 to 50% in 212 (56.6%), and of more than 50% in the remaining 44 (11.7%). Secondary infections, chiefly of the respiratory tract, occurred in near 33% of the patients.

Hypertonic saline solution, given intravenously in concentrations based on pretreatment serum electrolyte determinations was the principal treatment. The amount of fluids given per day per kilogram of body weight varied between 100 and 250 cc. Fluid retention 24 hours after the onset of rehydration therapy ranged from 1 to 10% of the total amount of fluids given to 206 patients, from 11 to 20% of that given to 91, and exceeded 20% of that given to 12. These figures do not include two patients who died within the first 24 hours and 64 who showed negative fluid balances in this period. Supportive antibiotic therapy, usually chloramphenicol, was given to all patients.

In this series 101 of the patients died, a case fatality rate of 26.93% as compared with 57.5% in 1956. This improvement is the result of earlier recognition and treatment and more accurate use of replacement solutions. In 65 of the fatal cases, death was caused by complicating infections. Thus the primary condition accounted directly for the death of only 9.6% of the entire group. No statistically significant relationships were found between the case fatality rates and the severity or duration of the disease prior to hospitalization, but the authors got the impression that the deaths were more closely related to severity than to duration. No significant relationship was observed between the case fatality rates and the volumes of fluid given per day per kilogram provided this was at least 100 cc. The case fatality rates in the few children given 301 to 380 cc. per day per kilogram did not differ significantly from those of the groups receiving the smaller, conventional quantities of fluids. No signs of overhydration were noted in such patients. No significant relationship was observed between the case fatality rates and the percentage of fluid retention following therapy, but none of the patients with over 20% fluid retention died. A notably higher case fatality rate was, however, noted in those patients coming to the hospital with clouded sensorium or in severe shock.

UNITED KINGDOM

Incidence of Sonne Dysentery.—Sonne dysentery is now a major public health problem in the United Kingdom, and in 1956 the number of reported cases reached its highest level, 49,009. W. H. Bradley and co-workers (*M. Officer* 99:175, 1958) noted this increase in incidence was accompanied a fall in the case fatality rate. In 1925, this rate was 39.1%, compared with 0.1% in 1956. In recent years, practically all the dysentery in England and Wales has been due to Shigella sonnei. The number of reported cases per 100,000 are much higher in the age group 0 to 4 (458.8 in 1956) than in the age group 5 to 14 years (288.5), and the incidence in the latter period was much higher than that observed in those 15 years of age or more (37.5). It is definitely a disease of the colder rather than the warmer months. Before 1947 it was relatively more prevalent in rural and similar areas, but lately it has been more prevalent in urban areas. As, unlike Shigella flexneri, the strains of Sh. sonnei are antigenically homogenous, no useful epidemiological information was obtained through serotyping of strains. Recently attention has been paid to the occurrence of sulfonamide-sensitive and sulfonamide-resistant strains. In many epidemics the strains of Sh. sonnei have the same sensitivities, but outbreaks in neighboring areas may have the same or different sensitivities. There is little support for the idea that a progressive replacement of sensitive by resistant strains is taking place. As in cases in which the strain is sensitive bacteriological cure is more easily and rapidly ensured if the patient is vigorously treated in the acute stage of the illness, it is recommended that, at intervals in an outbreak, organisms isolated from a small number of patients be tested for sensitivity to make sure that there has been no change and that they are sensitive to the preparations being used in treatment. Strains resistant to streptomycin and oxytetracycline have also been observed, but so far only infrequently.

A feature of Sonne dysentery is its clinical mildness, particularly in adults in whom the only evidence of infection may be one or two loose stools, with no other signs or symptoms. The frequency and extent of the spread suggests that the infecting dose of organisms is very small. Until recently attention has been focused mainly on day nurseries as places where the disease is spread. It has become increasingly apparent, however, that kindergartens are of great importance in the dissemination of the infection. The infected children pass the infection on to siblings and parents at home, although at times families may be the prime cause of spread of the infection. Except in special circumstances, there is little evidence to support the thesis that anything is to be gained from the addition of sulfonamide prophylaxis to the preventive measures normally used.

Coronary Thrombosis.—One of the few towns in which coronary thrombosis is reportable is Kilmarnock, a burgh of 44,000 inhabitants in Scotland. In his annual report, the local health officer stated that there were 110 coronary attacks in 1956. There were 74 first attacks, of which 50 were fatal, and 36 subsequent attacks, of which 15 were fatal. The available evidence did not suggest any connection between the excessive consumption of alcohol and coronary thrombosis. Most of the men were smokers, many of them heavy smokers, but in the case of women it was the exception to find any who smoked at all. Most of those affected were excitable rather than placid. Of the deaths among men 67% occurred within 24 hours of the onset, and the proportion in the women was even higher. While the number of men having a frank thrombosis as the first manifestation, as compared with anginal pains, was about equal, among the women nearly four times as many had thrombosis as a first manifestation as had anginal attacks. This was correlated with the fact that the mortality in women (33 of 40) was higher than that among the men (32 of 70).

Home Contacts of Poliomyelitis.—The Public Health Laboratory Service (*Month. Bull. Min. Health* 17:58, 1958) examined the stools of 96 patients with poliomyelitis and 290 household contacts in the summer and autumn of 1956. The finding of virus in the contacts was associated (1) not with the occurrence of paralysis in the patient but with the excretion of virus in the patient's feces and (2) with the age of the contact; the younger the contact, the more likely was virus to be found in the feces. Thus, under 5 years of age the proportion of excretors among the contact was 63%, between 5 and 15 years 36%, and over 15 years 9%. The proportion was higher in contacts of patients who were shown to be excreting virus than in those who were not (30%, compared with 18%). The elapsed time between the onset of illness in the primary case and the examination of feces from the contacts made little difference to the chances of finding the virus; the proportion was just as high in specimens examined three or four weeks after the onset as during the first week. Irrespective of which is the commoner method of infection, it seems clear that in any household in which one member develops poliomyelitis a large proportion of the other members are infected too. In children under 5 years of age this proportion probably approaches 100%. Whatever therefore may be said for segregating these children, there is practically nothing to be said for protecting them with gamma globulin.

Tuberculin Tests.—The tuberculin subcommittee of the research committee of the British Tuberculosis Association (*Tubercle* 39:76, 1958) compared the Mantoux, Heaf, von Pirquet, and jelly tuberculin tests. The comparisons were based on the effectiveness of the tests in detecting positive reactions, their reproducibility, their ease of performance, the consistency of the results recorded independently by two observers, and the confidence of the observer in the result recorded. On all of these points, the Mantoux and Heaf tests were found to be superior to the other two. On the other hand, blistering was more often recorded with the Mantoux and Heaf tests than with the other two. The jelly test was unreliable, difficult to perform, and hard to read. The sole recommendation of this test is that it requires no needle or skin puncture, but in the light of the accumulated evidence against it it should be abandoned. The von Pirquet test showed surprisingly poor results in this trial. The Mantoux test, using 5 units, yielded a slightly higher percentage of positives than the Heaf test. On the other hand, the Heaf test was preferred by 80% of the clinicians using both tests. Both tests gave highly reproducible results and showed little variation between the readings of the two observers. On the whole, the observers were more confident in their readings of the results of the Heaf test than in their readings of the Mantoux test, but this may be related to the fact that the Mantoux test result had to be recorded in millimeters and the Heaf test simply in one of four grades. Both tests with 5 units of tuberculin may therefore be regarded as being suitable as single tests for large-scale epidemiological work.

Psychosis due to Antituberculous Drugs.—E. H. Hare (*Tubercle* 39:90, 1958) reports a series of four patients admitted to a mental hospital on account of psychotic reactions attributable to the use of antituberculosis drugs. In one, confusion and choreiform movements arose after four weeks' treatment with streptomycin and persisted for four weeks after the drug was withdrawn. The second developed a toxic-confusional state after three weeks' treatment with streptomycin. This persisted for four weeks after withdrawal of the drug. In the third patient, auditory hallucinations and depression developed after four months of therapy with isoniazid and were still present two years after the drug had been withheld. The fourth patient developed auditory hallucinations after nine months' treatment with isoniazid. They persisted for six months after the drug was withdrawn. None of these patients had a previous history of psychotic or neurotic behavior, and only the fourth had a positive family history. It was concluded that if mental disturbance develops during antituberculosis treatment with streptomycin or isoniazid, it is reasonable to assume that the drugs may be responsible, and that, of the two drugs, isoniazid is more likely to be the cause and in general, therefore, should be the first to be withheld. Because psychosis associated with isoniazid may be prolonged, manifest mental changes in patients on isoniazid therapy should, in general, be an indication for withdrawing the drug.

Cycloserine in Pulmonary Tuberculosis.—On the basis of their experience with cycloserine in the treatment of 16 patients with advanced and drug-resistant cases of pulmonary tuberculosis, M. Weinberger and co-workers (*Tubercle* 39:96, 1958) concluded that cycloserine might be useful in patients who failed to respond to other forms of chemotherapy or whose tubercle bacilli were drug-resistant, but that great care was necessary in the selection of patients, and the dosage should not exceed 750 mg. daily. Of 11 patients in their series who completed three months of treatment, 10 improved clinically, 3 showed radiological improvement, and sputum conversion occurred in 1. Six showed a reduction of tubercle bacilli in the sputum after three months, but two of these reverted to their previous status in spite of therapy with cycloserine being continued Serious convulsions occurred in three patients, with one death. One other patient died of myocardial failure. but it is doubtful that his death was attributable to cycloserine. This drug has the advantage that it is effective by mouth without causing any untoward gastrointestinal symptoms, but the therapeutic dose is too close to the toxic dose for the drug to be used routinely, and it cannot be regarded as a substitute for standard antituberculous drugs.

Hazards of Mass Roentgenography.—In *Tubercle* (39:116, 1958) much criticism was expressed concerning a memorandum on the development of mass miniature roentgenography, published by the Ministry of Health last year. The main criticism was of the absence of any reference to the hazards of this procedure. Although the hazards may be small, there is a danger that chest physicians and surgeons may become careless about it. The dose received by the female gonads has already been shown to be greater for small films than for large ones, and the measurements so far for the skin dosage, comparing large and small films, have been found to be in a ratio of 1:4 or more. This should be taken into account in discussions as to whether large or small films should be used.

Boxer's 321 Days in Coma.—At an inquest at Manchester a verdict of death by misadventure was recorded on a 23-year-old boxer who died after being in a coma for 321 days after a bout. He had collapsed in his dressing room shortly after being felled by two blows on the jaw. He had previously sustained a head injury in an Army boxing match and had been warned to give up boxing on account of this. Two operations had been attempted on the brain. At the autopsy no fracture of the skull was evident and there was no laceration of the surface of the brain. The meninges were thickened and stained, suggesting a previous hemorrhage, but there was no sign of a recent one. Death was due [illegible] bronchopneumonia following internal hydrocephalus caused by traumatic subdural and subarachnoid hemorrhages. According to the pathologist the condition, which was comparatively rare, could have been caused by blows on the jaw.

Industrial Health Service.—In Slough, an industrial area just outside London, many factories are concentrated in a small area, which is suited for the establishment of the cooperative type of industrial health service. The Slough Industrial Health Service, which is independent of any national scheme, was started in 1947. The current annual report surveys the first 10 years' working of the service. When it began the membership included 52 firms with 6,324 employees. Now there are 179 member firms with 17,748 employees. The service provides medical care for those factories that are too small to support a full-time medical officer and nursing service. The medical care of employees of member firms with no medical department of their own costs about $6 a head per year. Half of this pays for the casualty service, which treats about 500 cases a day, 98% of whom are able to resume work after treatment. About 0.8% of those attending are referred for hospital treatment. An orthopedic surgeon, a plastic surgeon in charge of the hand clinic, a cardiologist, a dermatologist, and an industrial medical officer hold regular clinics. There is also a mobile dressing station which visits out-of-the-way factories and thus saves the time of the worker. The clinics are provided with roentgenological, pathological, physiotherapeutic, and social services. There is a rehabilitation center at Farnham Park. The health service also provides an occupational hygiene service, which, in collaboration with the London School of Hygiene and Tropical Medicine, advises on and investigates environmental conditions in the factories. Initial and periodic medical examinations and annual examination of senior executives are also carried out as part of the service.

Fat Mobilizing Factor in Urine.—Chalmers and coworkers (*Lancet* 1:866, 1958) showed that the urine of healthy fasting subjects contains a factor that mobilizes fat in experimental animals, increases the amount of fat in the liver, and increases the total metabolic turnover of body fat. It causes loss of weight without depressing appetite, the loss being in the form of body fat and water. Normal subjects fasted for 36 hours, and their urine was collected during the last 24 hours of this period. It was acidified to pH 5.3 and treated with 2 volumes of alcohol. The precipitate that formed in the next 24 hours was separated by filtration, washed, dried, and extracted with 0.5% sodium carbonate solution. The alkaline extract was reprecipitated at pH 5.3 with alcohol and the previous process repeated. The volume of extract was adjusted to 10 ml. for a 24-hour specimen. Mice, which were used as test animals, showed an increase of liver fat when given 0.5 ml. of the extract subcutaneously. With glyceryl tripalmitate, labelled with C^{14}, as a source of fat, it was shown that the extract did not merely transfer fat from the depots to the blood stream and liver but also increased the rate of fat metabolism in the body. After injecting the urine extract from normal subjects in the fasting state, not more than 25% of the administered activity of the glyceryl tripalmitate could be recovered as fat. As the total amount of fat in the animals was not less than in controls, it would appear that the total metabolic turnover of fat was increased in the animal as a whole. The injected mice also lost an average of 6 Gm. each over a 17-day period. Analysis of the carcasses and comparison with controls showed that this was due to loss of body fat and water. The active material was partially purified by paper chromatography. It was only present in the urine of fasting subjects or of subjects given a high fat or high protein diet. It was absent in those given a diet in which calories were supplied in the form of carbohydrate.

Allergic Reactions Abolished by Hypnosis.—The successful relief of the symptoms of allergic skin reactions by hypnosis was reported by Mason and Black (*Lancet* 1:877, 1958). A woman with a history of severe and intractable asthma and hay fever of 12 years' standing was found on skin testing to be sensitive to extracts of pollens of grasses, trees, and spring flowers. The attacks occurred only between May and July. As the patient refused desensitization an attempt was made to treat her by hypnosis. A week before the yearly attacks of asthma and hay fever were due she was put into a trance and told she would have neither asthma nor hay fever attacks in the coming season and that she would no longer be sensitive to skin tests for pollens and other substances in the atmosphere. Hypnotic treatment was given from April to July, and during the whole of this period the patient remained free for the first time in 12 years from attacks of asthma and hay fever. Weekly skin tests were made during this period with the allergens to which she was sensitive. The skin reactions slowly decreased each week until by the seventh week they could no longer be elicited in the arm, although they could in the thigh. Further suggestion was made that skin sensitivity would disappear over the whole body. This happened by the ninth week. An attempt was then made to elicit the Prausnitz-Küstner reaction in a nonallergic volunteer by intradermal injection of the patient's serum and subsequent skin testing with the allergens to which the patient was known to be formerly skin sensitive. After 30 minutes there was a skin response to extracts of pollen of grasses and trees. Thus with the patient now free from both allergic symptoms and skin reactions, it was still possible to produce the Prausnitz-Küstner reaction in the skin of a volunteer normally insensitive to the allergens. The symptoms of physical illness were removed by hypnosis, although the patient's blood still contained the serologic basis of her previous hypersensitivity in the form of passively transferable antibodies or atopic reagins.

Subsidized Medical Students.—Mr. Harold Edwards, representing the Royal College of Surgeons said that a different type of person is studying medicine today. Whereas 20 years ago only 27% of medical students received scholarships today 74% receive financial aid from government or university grants. The proportion is even higher among dental students. This results in selection of those who are apt scholars, but these students do not necessarily make the best physicians. The practitioner of today is not a mere machine. The art of medicine and surgery looks more and more to the basic medical sciences, and if the practitioner is to keep abreast of advancing knowledge he needs leisure to read, write, and travel. These are traditional obligations to his art, and they are expensive. He must therefore be able to look forward to a standard of professional earnings which allows him to incur such expenditure. If he is so "squeezed" that these essential activities are no longer possible, the quality and prestige of British medical and surgical practice will decline.

WORLD HEALTH ORGANIZATION

Poliomyelitis.—Virus diseases affecting the nervous system are a growing problem in Europe. Particularly regarding poliomyelitis, more information on the occurrence of the disease is needed. In many countries reliable data are not available and underreporting is general. To obtain a true picture of the importance of poliomyelitis it is necessary also to consider the accumulation of paralytic cases. Each year a new group of cases of permanent paralysis is added to the large numbers remaining from earlier years. The Study Group on the Control of Neurotropic Virus Diseases, which met in Copenhagen in April, recommended that the true medical, social, and economic consequences of poliomyelitis be determined.

Epidemic waves of poliomyelitis occur every few years and, because of this periodicity, it is too early to be quite certain about the value of mass vaccination campaigns against poliomyelitis, but the incidence of paralysis has declined after such campaigns, and this fact justifies the continuation of campaigns or the starting of new campaigns in countries where poliomyelitis is important. In countries where insufficient information is available more precise data should be obtained before an expensive vaccination program is undertaken. It will also be necessary to consider the results likely to be obtained in relation to the other demands on the limited resources available for health programs in some countries. Accidents after the use of poliomyelitis vaccine have been few because of the great care taken during vaccine production and testing. Although results with live poliovirus vaccines have been promising, these vaccines are still experimental and the group recommends caution in their experimental use.

Virus diagnostic laboratory services should be made available in all countries (1) to inform the public health authorities of disease-causing viruses existing in the country, which will enable them to take appropriate preventive action, (2) to assist in making epidemiological investigations and to improve the reporting of communicable diseases, (3) to evaluate control measures, and (4) to ensure the proper approach to prevention and the early treatment of disease. Though specific laboratory diagnosis of most virus diseases may be of little value for individual cases, an efficient laboratory service may be able to provide useful pointers to the physician in charge of the patient.

CORRESPONDENCE

ACCIDENTAL DROWNING

To the Editor:—It may be timely, with the swimming season about to start, to scrutinize the possible causes of accidental drowning. Being interested in recreational therapy for cardiacs, we at the Valley Forge Heart Hospital & Medical Center encourage water sports, among various activities, for patients with arrested rheumatic heart disease, hypertension, atherosclerosis obliterans, and congenital heart disease (classes I, II, A, and B, according to the classification of the American Heart Association). These activities are engaged in only under the careful supervision of the physician.

In reviewing records covering a period of 25 years at the Wolffe Clinic, Philadelphia, and the Valley Forge Heart Hospital, Fairview Village, Pa., with an average case load of 1,400 new cases per year, we found six instances of accidental drownings or near-drownings. On the basis of mere impressions, these accidents could have been attributed to heart disease. In all of these instances searching histories following the accident revealed preexisting grand mal and petit mal in cardiac and noncardiac patients.

In one patient, ventricular fibrillation was considered as a cause rather than an effect. No cardiac pathology was found at autopsy. The case of one oy may well illustrate the point. He drowned ile practicing in a university pool in June, 1956. n 1955, while attending another college, he had been considered one of the top free stylers in swimming history. In August, 1955, he had been in training for the Olympic tryouts and was one of the nation's brightest prospects.

In June of 1956, while training for the Olympics, he splashed to a stop in midstroke at the shallow end of the pool and grasped the gutter with both hands. He slumped back into the water with his eyes closed. Swimmers lifted him to the deck face down. He groaned a few times but did not respond to artificial respiration and the use of a Pulmotor. It was certified that the cause of death was "acute cardiac arrest while swimming." A physician from this school's department of health stated in a personal communication: "I am sorry to say that a careful scrutiny of the tissue at postmortem failed to uncover any suggestion of antemortem breakdown. It is assumed that ventricular fibrillation supervened, but the cause remains Deus Ex Machina."

The electrocardiogram of another patient after near drowning showed numerous ventricular ectopic beats occurring in rapid succession. This may be the mechanism which ushers in ventricular fibrillation when one or more ectopic foci assume control and become the cardiac pacemakers. Defibrillators may be lifesaving when available.

A young mother drowned in a bathtub while bathing her child. She had a slight mitral insufficiency but also suffered from grand mal. Yet, the death certificate read, "drowned during heart attack." Since there are more than half a million epileptics in the United States, it is unknown how many accidental drownings attributed to heart failure were due to grand mal and petit mal seizures while swimming or being near water.

Since an accidental drowning, apparently due to an epileptic seizure, in a Y.M.C.A. pool, the director of physical education does not permit epileptics the use of the pool, regardless of individual or parental pressure. Students in the field of epilepsy feel that this is not warranted, particularly when the physician has the patient under good medical control. According to some authorities, epileptics under supervision are safe where normal persons are completely safe. However, a very careful history, particularly in reference to recurring convulsive seizures, might be one way of reducing the number of accidental drownings.

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STAPHYLOCOCCIC INFECTIONS

To the Editor:—Recent articles in The Journal on staphylococcic infections in hospitals have been widely discussed. This situation should give an important warning to physicians regarding hospitalization of patients for diagnostic studies. There probably is some risk to such patients. Therefore physicians should think twice before hospitalizing patients on some nebulous diagnosis in order to get an insurance company to pay for a diagnostic examination that could well have been done on the outside. We physicians, without being alarmists, can gently wean patients away from such unnecessary hospitalization.

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MISCELLANY

AMERICAN COLLEGE OF PHYSICIANS MEETING

Once again the chemotherapeutic revolution of the last 15 or 20 years came under the close scrutiny of the American College of Physicians. Dr. Howard Wakefield, of Chicago, was emphatic in condemning routine use of any drugs. When medicine can be practiced by formula it ceases to be an art or a science and becomes merely skilled labor. Individualization is essential in treating any condition, because no drug has the same effect on all persons and may even have different effects on the same person at different times. He particularly condemned the routine use of anticoagulants and emphasized the need for careful differentiation between the pain of a coronary occlusion and that of a perforated peptic ulcer, since more than one patient with the latter condition has suffered a fatal hemorrhage as a result of taking anticoagulants. In a panel on the tranquilizers, it was noted that, although these drugs are indicated chiefly in the treatment of psychoses, they have come to be used on millions of nonpsychotic patients. Dr. Edward Weiss, of Philadelphia, said that often a physician develops a feeling of hostility toward a patient who has a functional illness or an illness that does not respond promptly to treatment. In such a situation there is a great temptation to give the patient a tranquilizer. This amounts to putting the patient in a chemical strait jacket and is a highly questionable procedure. Dr. Weiss concluded that the more a physician gives of himself the less need he will have to prescribe tranquilizers.

A similar note was struck by the panel on life situations, emotions, and the gastrointestinal tract; it was concluded that, when a patient shows antagonism to a physician by such complaints as "I've been coming to you for a long time and I'm not a bit better," the physician must not react in kind by rejecting the patient. He must not, for example, say, "Well, then, why don't you go to someone else?" or "I have done all that I can for you." Surely, no physician is likely to react in this way toward a patient he knows is dying of cancer. Refusal to reject the patient is in itself a powerful therapeutic tool. When there is a genuine feeling for the patient's welfare, the patient senses this and is thereby given a support he greatly needs. Another potent therapeutic measure that should never be omitted is to give the patient a simple physiological explanation of the cause of his symptoms couched in language he can understand.

In delivering the John Phillips Memorial Lecture, Dr. Amos Christie, of Nashville, Tenn., said that since the introduction in 1945 of the histoplasmin skin test as a case-finding tool and as a means of establishing an epidemiological index human histoplasmosis has emerged from a category of rare disease to one which must be considered in any case where hepatosplenomegaly, fever, ulceration of the skin and mucosa, and pulmonary lesions are otherwise unexplained. Prior to 1945, histoplasmosis was considered to be a uniformly fatal disease. It has now been established that there are many benign but symptomatic cases, and these are frequently recognized when one's index of suspicion is high and when currently available laboratory aids are used. The geographic distribution is also much wider than previously recognized. Histoplasmotic meningitis simulates the meningitis of tuberculosis. Histoplasmotic involvement of the adrenals has also been observed. The only chemotherapeutic agents of any value are some of the sulfonamides.

Influenza.—Dr. Gordon Meiklejohn, of Denver, stated that the chief problem remaining to be solved in influenza appears to be that of preparing a vaccine that would protect not only against influenza virus strains current in the past but also against new variants. The situation which existed when Asian strains of influenza A were first isolated appeared particularly promising because there was time to prepare in advance a strictly homologous vaccine for the epidemic that was expected. It soon became clear, however, that with vaccines for Asian strains of potency comparable to those used in earlier studies in single injections the antibody response was far less satisfactory than had been anticipated. In retrospect, it is clear that the schedule of single-injection immunization which has been followed in the past was unsatisfactory and that a double or booster type of immunization schedule produced a far better antibody response. Time did not permit the use of this type of program. It was concluded that the most promising approach to protection against any type of influenza A or B would be to prepare a vaccine containing all the major families of each virus. If there are only four or five main families within the influenza A group this would not be too formidable a task, as polyvalent adjuvant vaccines could be used to provide immunization against these major families. Appropriate booster injections could then be given at suitable intervals and a much higher degree of protection obtained in the future than has been observed in the past.

Apoplexy.—Harold Stevens, of Washington, D. C., reported that the spontaneous occurrence of cerebrovascular accidents in normotensive, apparently healthy persons is not as rare as was once believed. He encountered 32 such cases in young adults and 2 in children. Acute hemiplegia and other focal neurological manifestations characterized this group. All subjects were ambulatory and active. Most were white-collar workers. Although of 1 of the triiodothyronine preparations along with thyroxin or desiccated thyroid. Triiodothyronine was withdrawn in 1 patient after a few days because of side-effects. Three patients were treated for 1 month, and the remainder for 2 months or more before the therapeutic effect was evaluated. Eight patients were treated with triiodothyronine for at least 6 months, and 2 for more than 1 year.

The condition of 13 patients was improved and that of 17 was unimproved or became worse. Side-effects occurred in 9 of 34 trials and could not always be eliminated by decreasing the dosage. The highest percentage of good response occurred in a small group (4 of 5) who received a combination of desiccated thyroid or thyroxin with supplemental triiodothyronine. Despite careful analysis of the data, no basis was found on which to predict which patients would receive benefit from the triiodothyronine. However, the occasional improvement, sometimes dramatic, suggested that a therapeutic trial with triiodothyronine in difficult or unresponsive cases of hypometabolism or hypothyroidism is justified.

Idiopathic Renal Glycosuria in Three Generations with High Incidence. E. Gjone. Nord. med. 59:306-307 (Feb. 20) 1958 (In Norwegian) [Stockholm].

In the family studied, a man in the first generation and his 4 children and 2 of the 5 siblings in the third generation have renal glycosuria, and a third probably also has a low renal threshold. None have symptoms of diabetes mellitus or blood sugar curves which might point toward diabetes mellitus. Renal glycosuria is usually an asymptomatic condition. In some cases there may be fatigue or lack of tone, and glycosuria as such may give local symptoms due to genitoanal infections. Apart from therapy directed to the local symptoms, the condition does not require treatment. Diagnosis is important for the patients, so that they may know that neither change in the way of life nor dietetic measures are necessary; they will also know that they do not have any form of diabetes mellitus and are not more predisposed than other persons to develop this disease.

Circulatory Changes in Chronic Liver Disease. J. F. Murray, A. M. Dawson and S. Sherlock. Am. J. Med. 24:358-367 (March) 1958 [New York].

The authors studied the circulatory changes in 24 patients with chronic portal cirrhosis, in 6 patients with chronic biliary cirrhosis, and in 6 patients with extrahepatic portal vein obstruction and compared the findings in these 36 patients with those in 14 normal persons. Twelve of the 24 patients with portal cirrhosis had a cardiac index above the upper limit of normal. Clinically, these patients had evidence of increased peripheral blood flow and ejection systolic murmurs. Roentgenographic or electrocardiographic changes were uncommon. Patients with biliary cirrhosis and portal vein obstruction had normal cardiac indexes. An increased total blood volume, mainly plasma volume, was found in patients with portal cirrhosis who had an increased cardiac index, a large portal-systemic collateral circulation, arterial oxygen desaturation and low serum albumin levels. The increased portal venous network did not account for the increased blood volume in portal cirrhosis, as patients with extrahepatic portal vein obstruction had virtually normal blood volumes. The low serum albumin levels may, in part, represent the dilution of a normal amount of circulating albumin by an increased plasma volume. Four of the 24 patients with portal cirrhosis had low arterial oxygen saturation. Cardiac catheterization data in 1 patient and pulmonary function studies in 2 others suggested that the arterial desaturation may have been due to the shunting of blood through pulmonary arteriovenous anastomoses. The case of 1 of these patients is presented in detail.

In most patients with portal cirrhosis the increased cardiac output was tolerated without evidence of decompensation. Congestive heart failure was present in 1 patient reported on in detail. As liver functions and the clinical status of patients with portal cirrhosis improved, the cardiac output returned to normal. The mechanism of production of the hyperdynamic circulatory state in portal cirrhosis is unknown. There is profound vasodilatation, and the mechanism of this is discussed. No specific therapy is indicated for patients with a hyperdynamic circulation unless decompensation is present. Therapy should be directed to improving the underlying liver disease.

Muscular Dystrophy: Evaluation of Adrenal Cortical Function and Influence of Corticotropin, Cortisone and Testosterone. L. J. Soffer, J. Geller and J. L. Gabrilove. Metabolism 7:97-107 (March) 1958 [New York].

Three women, between the ages of 50 and 55 years, with dystrophia myotonica and 1 35-year-old man with progressive muscular dystrophy of the facioscapulohumeral type were studied by the authors in an attempt to ascertain the status of adrenal cortical function in patients with muscular dystrophy of both the progressive and the myotonic type. The authors also wished to investigate the influence of corticotropin, cortisone, and testosterone on such biochemical parameters as creatine and creatinine excretion, serum and urine amino acid levels, organic phosphate excretion, folic acid and vitamin B_{12} metabolism in patients with this disorder and to observe the clinical effect of hormone therapy. Two of the women with dystrophia myotonica and the male patient with the facioscapulohumeral form of dystrophy were given corticotropin for short periods in either the lyophilized aqueous form or as a repository corticotropin (ACTH) preparation. The same 3 patients were subsequently given cortisone orally. The duration of treatment varied from 4 to 16 months. The third woman with dystrophia myotonica received testosterone propionate and testosterone enanthate in sesame oil (Delatestryl) by intramuscular injection for 4 months. All the patients, with the exception of the third woman, received in addition 40 Gm. of gelatin administered orally daily.

The 2 patients with dystrophia myotonica treated with adrenal steroids and corticotropin showed striking improvement in the myotonia and subjective well-being, gaining 20 to 33 lb. in weight, and were able to engage in muscular activities previously impossible. The patient with dystrophia myotonica who was given testosterone showed little change objectively and subjectively. The patient with facioscapulohumeral dystrophy treated with cortisone remained unchanged.

No uniformity was observed in the results of the adrenal cortical function studies in the patients with dystrophia myotonica. In 1 woman, the changes obtained in the 24-hour urinary excretion of the neutral 17-ketosteroids and formaldehydogenic corticoids and in the plasma 17-hydroxycorticoids after stimulation with corticotropin indicated impaired adrenal function. The second woman with dystrophia myotonica revealed an inadequate adrenal cortical response to the intra- scular administration of corticotropin, as meas- d by the 24-hour urinary excretion of the neutral 17-ketosteroids. The urinary and plasma glycogenic corticoid responses to the administration of corticotropin were adequate in this patient. It may be concluded that some abnormalities in adrenal cortical function existed in both these patients. Adrenal function was normal in the third woman with dystrophia myotonica and in the man with facioscapulohumeral dystrophy. Corticotropin, cortisone, and testosterone did not influence creatine tolerance in any of the 4 patients. The urinary organic phosphate excretion was reduced in all patients given corticotropin and cortisone. In the 1 patient treated with testosterone, there was no change in the urinary excretion of organic phosphate. No conclusions concerning the effect of corticotropin, cortisone, or testosterone on amino acid tolerance could be drawn from the authors' studies. The vitamin B_{12} and folic acid blood levels were normal in all patients and remained uninfluenced by corticotropin therapy.

The Geographic Distribution of Coccidioides Immitis and Possible Ecologic Implications. K. T. Maddy. Arizona Med. 15:178-188 (March) 1958 [Phoenix].

The Lower Sonoran Life Zone, one of several biological regions into which the United States have been classified, is characterized by arid and semiarid climates, with hot summers and few winter freezes, a low altitude and an alkaline soil. This limits plants and animals to certain types that can survive in this environment. It is the only environment which seems to permit Coccidioides immitis to exist in nature. Presumably the fungus grows primarily in the soil. A preliminary study of the plant and animal association within the Lower Sonoran Life Zone in relation to areas of varying endemicity for coccidioidomycosis, carried out by the author in Arizona, New Mexico, Texas, Utah, Nevada, and California, revealed a close correlation between the geographical areas of the Lower Sonoran Life Zone and the known endemic areas for coccidioidomycosis in the United States. July mean temperatures from 80 F to about 90 F, January mean temperatures from 39 F to 53 F, and an annual rainfall of about 5 to 20 in. seem to be the most ideal for the propagation of C. immitis in nature. The parts of the Lower Sonoran Life Zone with a more or less arid climate or with lower summer mean temperatures are apparently less favorable areas for the fungus to propagate. Thus, some areas of the Lower Sonoran Life Zone that had not been delineated as endemic areas for coccidioidomycosis are now so designated by the author who carried out coccidioidin tests on home-raised cattle in these areas. Other areas in which C. immitis infections could be expected to occur have also been designated.

Patient Accidents Occurring in Hospitals: Epidemiologic Study of 614 Accidents. H. M. Parrish and T. P. Weil. New York J. Med. 58:838-846 (March 15) 1958 [New York].

The authors investigated all accidents occurring among the inpatients at the Mount Sinai Hospital in New York City (a large general hospital) during one calendar year. The accident report forms of the hospital were used for this investigation. There were 614 accidents among 23,911 admissions during the year studied, an annual incidence of 25.7 per 1,000 patients. [In addition, the authors estimated that between 300,000 and 550,000 patient accidents occur each year in American hospitals.] The accident rates were more than twice as high among male patients as among female patients. The rate among ward patients was 42.5 per 1,000 as compared with a rate of 17.3 for semiprivate and 13.5 for private patients. Accidents per 10,000 days of patient exposure were found high among the very young, under 1 to 9 years of age, and among adults, aged 40 to 79. Fortunately, approximately 45% of patient accidents resulted in no detectable injury, and less than 5% resulted in a serious injury or death. With the exceptions of falls from bed and falls in the bathroom, all types of accidents occurred more frequently during the hours from 6 a. m. to 6 p. m. Approximately 70% of all accidents occurred within a 10-ft. radius of the patient's bed. Faulty physical equipment and hospital personnel played contributing roles in less than 10% of the accidents.

Falls from bed were the most frequent type of accident and accounted for 283 (46%) of all accidents. Of 283 falls from bed, 106 happened while bedrails were in place. In the opinion of these authors, beds and side-rails now in use are not designed for safety. Most beds are too high for a patient to get in and out of bed without risking a fall and subsequent injury. Bedrails are ineffective in keeping many irrational and restless patients confined to bed. The authors believe that safely designed beds and effective side-rails or restraints would reduce both the frequency and the severity of bedside accidents. Defects in the patient's mental, emotional, and physical status were prominent among the causative factors for accidents and were difficult to control. Only about 50% of the patients were completely alert and rational at the time of the accident. Patients with defects of their neuromuscular or skeletal systems and those with advanced cancer and heart disease were especially susceptible to accidents. Patients who have received sedatives, narcotics, or anesthetics require special care. Rubber airways are preferable to metal ones. Many accidents involving wheel chairs and crutches could have been prevented by instructing patients on how to use them properly. Personnel should assist elderly, crippled, and senile patients to the bathroom and to bed. What is needed is a team approach, one in which a hospital administrator, a physician, a nurse, an epidemiologist, a safety engineer, and a biostatistician coordinate their efforts. Patient accidents conform to a definite epidemiologic pattern. They can be prevented in many instances.

Universal Edema After Diabetic Precoma Treated with Thiamine. T. Deckert. Ugesk. læger 120:224-226 (Feb. 13) 1958 (In Danish) [Copenhagen].

From the 4th to the 14th day after treatment for diabetic precoma a woman, aged 24 years, developed universal massive edema, with weight increase of 18 kg. (39.6 lb.). There were no signs of cardiac, renal, or hepatic disease; no disturbance of the electrolyte balance was demonstrable. On intensive thiamine therapy the edema disappeared in 7 days, with loss of 13 kg. (28.6 lb.) in weight. Thiamine deficiency is thought to have been the essential cause of the edema.

SURGERY

Grave Cerebral Fat Embolism: Treatment and Prognosis. P. Heimann. Nord. med. 59:260-262 (Feb. 13) 1958 (In Swedish) [Stockholm].

Two cases of massive fat embolism are described. The first patient was admitted with fractures of the right thigh and right upper arm and facial injuries; the second, with fractures of the left leg and thigh and right upper arm. Both patients had marked symptoms in the pulmonary circulation and in the cerebral vascular system. The clinical picture was alarming. The patients were successfully treated with chlorpromazine in large doses (400 mg. intramuscularly administered daily). Antibiotic treatment, exact fluid balance, and in one case tracheotomy were features of the intensive treatment during the acute phase. Later, open reduction of the fractures was accomplished. No side-effects followed the administration of chlorpromazine. On follow-up no remaining symptoms from the cerebral fat embolism were demonstrable. There seem to be no late cerebral complications even after massive fat embolism. After 4 to 6 months the patients showed no signs of cerebral damage or other neurological symptoms.

Chemopallidectomy and Chemothalamectomy for Parkinsonism. I. S. Cooper, G. J. Bravo, M. Riklan and others. Geriatrics 13:127-147 (March) 1958 [Minneapolis].

The authors performed operations on the basal ganglions in 600 selected patients with Parkinsonism. Twenty-one per cent of the patients had serious psychological abnormalities, 5% had latent schizophrenia, and 14% showed signs of organic mental disease. Fifty of the patients were subjected to occlusion of the anterior choroidal artery. In 550 patients destructive lesions of the globus pallidus or the ventrolateral nucleus of the thalamus were produced by the injection of a neurolytic agent, either dehydrated alcohol or an 8% solution of a specially prepared cellulose in 95% ethyl alcohol (Etopalin). Five hundred consecutive patients with Parkinsonism, who for various reasons were not operated on, served as a reference group.

Favorable results were obtained with occlusion of the anterior choroidal artery in 35 of the 50 patients with far-advanced and incapacitating Parkinsonism. In many patients both tremor and rigidity as well as long-standing postural deformities were completely abolished. These patients were followed closely for 5 years without recurrence. Favorable results were obtained in somewhat more than 70% of the 550 patients treated by chemopallidectomy and chemothalamectomy. There was objective alleviation of tremor, rigidity, and incapacitation without infliction of any neurological deficit. In certain patients there has also been improvement in masked facies, elevation of mood, decrease in greasiness of the skin, and, in rare instances, mitigation in oculogyric crises. The mortality rate in the 600 patients was 3%, with a 2% incidence of hemiplegia. About 10% of the patients showed signs of involvement of the pyramidal pathways in a transitory form, but these signs abated somewhat within 3 to 6 weeks after the operation. About 20% of the patients with operation on the dominant hemisphere of the brain had transitory speech difficulties during the acute postoperative period, but lasting aphasia was produced only in 2. Most speech difficulties have been related to placement of the trephine opening too far posteriorly. When operating on the dominant side of the brain, the bur hole should be placed anterior to the coronal suture.

Because of the extremely variable and protean symptoms of Parkinsonism, one must select patients only after painstaking evaluation. The ideal candidate for surgical intervention is one who has unilateral tremor and rigidity. Bilateral Parkinsonism can be treated by performing the surgical intervention on the basal ganglions first on 1 side and at least 6 months later on the other side of the brain. In patients of advanced age it is deemed advisable to operate only on 1 side, even though the patient may have bilateral symptoms. In the early stages of the authors' investigation, occlusion of the anterior choroidal artery was confined to totally incapacitated patients, but as techniques became more certain and the risks became minimal, it became possible and desirable to perform chemopallidectomy and chemothalamectomy on patients in an earlier stage of the disease. With the intro- tion of a brain needle or cannula with 2 lumens ugh a small trephine opening in the skull un- er roentgenographic control provided by iophendylate (Pantopaque) combined with the neurolytic agent, and with a small inflatable balloon at the extremity of the cannula, to which 1 of the lumens leads, it is possible to produce an accurately localized lesion and to perform a physiological test by balloon inflation in the globus pallidus or thalamus in the conscious, cooperative patient. Thus, the result can be predicted before infliction of a permanent lesion. The indwelling brain-cannula technique allows the surgeon to tailor the size of the lesion to the needs of a particular patient. Contraindications to surgery are as follows: organic mental deterioration, psychosis, or pseudobulbar palsy with inability to swallow or speak; excessive vegetative symptoms, such as hyperpyrexia, hypersalivation, and flushing of the skin; physiological old age with marked evidence of arteriosclerosis in a patient who appears much older than his stated age; and ordinary medical contraindications, such as cardiac or renal failure or extreme hypertension.

Intravenous Cholangiography in Detection of Stone-bearing Cystic-Duct Remnants (So-called Re-formed Gallbladders). J. E. Berk and R. N. Lee. Am. J. Digest. Dis. 3:220-228 (March) 1958 [New York].

The authors report on 6 women, between the ages of 38 and 68 years, who had undergone cholecystectomy for severe epigastric pain, who began to have symptoms similar to those experienced before the cholecystectomy, and in whom a stone-bearing dilated cystic-duct remnant or so-called re-formed gallbladder was revealed by intravenous cholangiography. These 6 cases of stone-bearing re-formed gallbladder were detected among routinely performed intravenous cholecystocholangiographic studies at the Sinai Hospital in Detroit within a period of 22 months. These observations suggest that stone-bearing cystic-duct remnants occur more often than has been generally appreciated; they also emphasize the need to explore the biliary ducts diligently for calculi at the primary cholecystectomy and to remove the entire gallbladder and as much of the cystic duct as possible.

Indications to Radical Surgical Intervention in Patients with Carotid Body Tumors. M. Wenzl. Klin. Med. 13:49-53 (Feb.) 1958 (In German) [Vienna].

The author reports on a 40-year-old woman with a carotid body tumor on the right side of the neck, which had been growing slowly for 13 years until acceleration of growth was causing considerable difficulty in breathing and a disturbing throbbing in the neck and ear. Surgical intervention revealed a tumor which was sharply limited by a capsule and which surrounded the carotid bifurcation so intimately that its removal seemed to be possible only with simultaneous resection of the vessel. Both the external and the internal carotid arteries were almost completely compressed by the tumor. Compression of the common carotid artery for 20 minutes did not cause any symptoms, and extirpation of the tumor was decided on. Microscopic examination of the operative specimen revealed a paraganglioma. Three days after the operation hemiplegia occurred on the left side, but improvement resulted rapidly from various vasodilator procedures and repeated stellate ganglion blockade. Complete return to health resulted from further after-treatment at a hospital for nervous diseases.

The risk of the resection of the carotid bifurcation which was passing through the tumor seemed to be less severe, since the slowly progressing compression of the blood flow in the internal carotid artery suggested an accommodation of the brain to the reduced blood perfusion. This seemed to warrant effective protection against cerebral complications. Despite the relatively favorable circumstances, the reported case has clearly shown that neither the compression of the common carotid artery carried out in the course of the operation without causing symptoms nor the compression of the carotid bifurcation by the tumor itself may prevent with certainty the occurrence of temporary cerebral complications. The author, therefore, advises against an aggressive surgical intervention on carotid body tumor, since these tumors are nearly always benign, show a slow growth, and are causing relatively few symptoms. Only increasing complaints caused by displacement of adjacent organs justify surgical intervention. Radical extirpation of the tumor with simultaneous resection of the carotid bifurcation is associated with an enormous risk and should, therefore, be performed only in exceptional cases in which, besides the rapidly accelerated growth of the tumor and corresponding clinical symptoms, adequate cerebral circulation has been assured by the compression of the vessels depending on the tumor or by restoration of the circulation with the aid of anastomosis of the vascular stumps of the carotid artery. Definite proof of malignant degeneration is of only theoretical significance as an indication to radical surgical intervention because of the rarity of such an occurrence.

Indications and Results of Ligation of the Internal Mammary Arteries in the Treatment of Coronary Insufficiency. G. Gucci. Riforma med. 71:1438-1441 (Dec. 14) 1957 (In Italian) [Naples].

The author advocates ligation of the internal mammary arteries as a prophylactic measure in the management of mild subacute or chronic coronary insufficiency to anticipate the grave form of the disease. Originally this procedure was employed for treatment of an infarct of the myocardium and of angina pectoris. Twelve patients with mild coronary insufficiency were operated on by performing 24 ligations during the last year. Disappearance of anginal pain was noted in all patients. The relief indicated that a revascularization process had taken place. Schellong's test for circulatory function showed improvement in all patients. Electrocardiographic findings also showed tendency toward normalization of circulation in many patients. Signs of preceding infarctions remained unchanged. The postoperative course was uneventful, and no recurrence developed.

Ligation of the internal mammary arteries for treatment of coronary insufficiency may not be used as a procedure of urgency or after chemotherapeutic measures have been exhausted, but rather as an adjunct to other therapeutic procedures for treatment of coronary sclerosis. There are few contraindications to this operation, and they are related to the cardiac, rather than to the general, state of health. The best time for this operation is 5 to 6 months after an infarction, when the lesion has cicatrized and the hemodynamic function has stabilized.

Aneurysm of the Abdominal Aorta. K. N. Morris. Australian & New Zealand J. Surg. 27:183-192 (Feb.) 1958 [Melbourne].

Morris discusses the clinical aspects and the management of aneurysm of the abdominal aorta, pointing out that rupture of the aneurysm is a common terminal event and that operation should be undertaken, if possible, before rupture occurs. In 15 of the 24 patients observed by the author, the aneurysm had already ruptured. Among the 9 patients in whom the aneurysm had not yet ruptured, there were 2 who did not have any symptoms. One of these was an 82-year-old woman, and the other was a man in poor general condition. In both of these instances operation was not recommended. There were only 2 patients who were classed as "good risks." One had mild symptoms, and the other had pain suggestive of impending rupture. Operation was undertaken in both of these. The first patient did well; the second died of a coronary occlusion 6 days after operation. The remaining 5 patients were all in the "bad-risk" category for such reasons as angina pectoris, severe hypertension, auricular fibrillation, and cardiac failure. These patients were subjected to operation because of intolerable pain or threatened rupture. Two died, and 3 survived.

Of the 15 patients on whom operation was performed after rupture, 6 are now alive after periods varying from 5 to 30 months. It is difficult to imagine a group of patients who would constitute a worse operative risk than this. The salvage rate is low, but, in view of the almost certain fatal outcome if untreated, even this low rate is worthwhile. The causes of death were mainly related to the patient's age, the condition of his cardiovascular system, and his kidneys. It cannot be anticipated that operations of this magnitude, carried out on this type of patient, can ever be uniformly successful. The author comments on various operations for aneurysms of the abdominal aorta. The tabulations of his own cases show that he used a nylon prosthesis, particularly in the operations that were performed prior to rupture but also in some of those performed after rupture. Homograft replacement and reconstruction of the aorta from the wall of the aneurysm were employed in other patients.

A Clinical Trial of Prednisolone in Bone and Joint Tuberculosis. A. J. M. Cathro. East African M. J. 35:31-35 (Jan.) 1958 [Nairobi, Kenya].

The idea behind the present investigation was to administer prednisolone along with antituberculous drugs in cases of bone and joint tuberculosis in the hope that this therapy would enhance the effect of the antibiotics by removing and inhibiting the formation of fibrous tissue. It seemed possible that such a regimen might facilitate operations on the affected joints or even do away with the need for radical surgery altogether. Sixteen patients with active tuberculosis of bone and joint were chosen at random. Their ages ranged from 4 to 47 years, the average age being 16 years. Ten patients were given prednisolone, and 6 served as controls. In the test series, after the diagnosis and a clinical evaluation had been made, antituberculous therapy in the form of streptomycin and isoniazid was begun. After an interval of 1 to 2 months, depending on the progress, prednisolone was given for 2 months, chemotherapy being continued meanwhile. In view of the danger of delayed wound healing, surgery was postponed in those patients requiring it for 1 to 2 months after the withdrawal of prednisolone. In the control series the patients were observed over a corresponding period of time under the influence of streptomycin and isoniazid alone. Antituberculous therapy was maintained in the usual way after treatment with prednisolone and in both series after surgery.

The daily doses for adults were 1 Gm. of streptomycin, 0.6 Gm. of isoniazid, and 20 mg. of prednisolone, the last 2 treatments being given in divided doses. Children were given proportionately smaller doses. Of the 10 patients treated with prednisolone, 7 had tuberculosis of the spine, 6 in the lumbar region and 1 in the thoracic region; 2 had tuberculosis of the knee joint; and 1 had tuberculosis of the hip joint. In the group with spinal disease, 2 patients had an active pulmonary lesion as well, 1 had chronic tuberculous arthritis of the right carpus, and 1 had paraplegia of a year's duration. One patient with tuberculous arthritis of the knee had a calcified pulmonary lesion. The limited number of patients does not permit a definite opinion the effect of prednisolone. The findings at operation disproved the idea that prednisolone is a solvent of pathological fibrous tissue. Prednisolone did not prevent bone absorption or sequestration. It may have been a factor in speeding up new bone formation in some of the patients observed. There would appear to be no contraindication to the use of prednisolone in active tuberculosis or osteoporosis, as is commonly stated. There is no conclusive evidence that prednisolone facilitates or obviates surgical intervention in bone and joint tuberculosis.

Biliary Tract Surgery in Retrospect. A. Cass, K. Glass and J. Smith. Australian & New Zealand J. Surg. 27:193-203 (Feb.) 1958 [Melbourne].

The first part of this discussion is concerned with certain aspects of the operations for calculi of the biliary tract performed on 180 patients. Twenty-two (12%) of the operations were for acute complications. The authors differentiate between "acute compulsory" (rupture of the gallbladder) and "acute elective" cases. No "acute elective" operations were done until it was seen that the over-all mortality in the first 100 operations was 1%. Most of the operations for acute conditions were, therefore, among the last 80 patients. No elevation of the mortality rate occurred. During this period occasional patients with acute complications have not been subjected to immediate surgery if superadded conditions, such as congestive cardiac failure, were present. The cholecystostomies were performed on patients with ruptured gallbladders whose condition was so parlous that the anesthetist demanded speed. The choledochostomy rate was 35%; stones were found in 60% of the ducts opened. This means that in 22% of all the patients in this series 1 or more stones were found in the common bile duct. The addition of choledochostomy to cholecystectomy did not elevate the mortality rate. Choledochostomy is required so frequently in biliary tract surgery that there is no place for the cholecystectomist who rarely, if ever, performs it. The removal of all stones in the bile ducts (Lahey's "third stage") has not yet been achieved. The percentage of patients having stones in their common bile ducts at operation is obviously bound up with the range of the indications for biliary tract surgery. If these indications are extended to include (for example) noncalculous cholecystitis, then a lower percentage of common bile duct stones is likely.

The second part of this paper is concerned with a follow-up study of 951 patients, which revealed that there are trustworthy indications for biliary surgery, less trustworthy ones, and some common mistakes. The trustworthy indications are biliary colic, obstructive jaundice, and acute cholecystitis. The less trustworthy ones are dyspepsia (because 2 in 3 cases recur), a "positive" Graham test, incidental stones (e. g., found at laparotomy), and the fear of cancer. The common errors are peptic ulcer and operating for pains which are not biliary colic (e. g., due to spondylitis). Biliary colic, jaundice, and dyspepsia were studied during the follow-up. The authors also evaluated the likelihood of the development of cancer or of symptoms in those with symptomless gallstones. It was found that undue reliance on Graham's test can result in a cholecystectomy being performed when the only lesion present is a peptic ulcer. This survey showed that the postcholecystectomy syndrome is a confusing concept. Ideas on postcholecystectomy syndromes are determined by what surgeons expect of the operation. For example, the gallbladder may be removed because the patient has biliary colic plus dyspepsia, and the dyspepsia persists after the operation. The authors disagree with certain views expressed by American surgeons. They regard as doubtful the following statements: (1) "Calculous cholecystitis, whether symptomless or not, is an indication for remedial surgery"; (2) "gallbladder disease should be eradicated before patients reach old age and develop complications, such as jaundice, acute inflammation, or malignancy"; and (3) "they ['the silent gallstones'] should be removed before the shriek of malignancy." The survey suggests that not only is this language extravagant but the ideas behind it are also.

The Treatment of Acute and Chronic Ulcerative Colitis. C. H. Brown. Am. Pract. & Digest Treat. 9:405-411 (March) 1958 [Philadelphia].

The author reports his experience with the management of patients who had nonspecific, idiopathic, ulcerative colitis. The exact number of patients who were treated medically is not given. Twelve patients were given steroids for relatively short periods of time (10 to 30 days). Surgical treatment was given to 211 patients. The 2 basic fundamentals of medical treatment are rest and food. Rest should include complete mental, emotional, and physical relaxation. A high-protein, high-carbohydrate, high-caloric, and low-residue diet is imperative. If the patients is unable to eat, parenterally administered fluids must be given. It frequently is difficult to give the required daily amount of 3,500 calories parenterally, and, therefore, a continuous drip of eggnog, amino acids, and protein and carbohydrate supplements may be administered with the aid of a stomach tube. If the patient is able to eat, his daily diet is increased to 3,500 calories with 150 Gm. of protein. Stimulation of the appetite with small doses of insulin before meals may help. Antispasmodics, such as atropine and belladonna, can be given to rest the colon. The potent anticholinergic drugs, such as methscopolamine (Pamine), propantheline (Pro-Banthine), and diphemanil (Prantal), are more effective in decreasing gastrointestinal motility. The most important supportive measure is the transfusion of whole blood. Supplemental vitamins administered in rather large doses are necessary and should include vitamins A, D, C, and the entire vitamin B complex. The administration of minerals and electrolytes, such as calcium, iron, sodium, chlorides, and potassium, may be necessary in severely ill patients. Oxytetracycline (Terramycin), given in doses of 250 to 500 mg. 4 times daily, and the other antibiotics may be of help in controlling secondary infection. The nonabsorbable sulfonamide preparations, phthalylsulfathiazole (Sulfathalidine) and succinylsulfathiazole (Sulfasuxidine), are of particular value in ulcerative colitis, and tablets of 2.5 Gm. 4 times daily may be given for long periods of time. Eighty-seven per cent of the patients with ulcerative colitis made satisfactory progress on this medical program.

The author's experience with steroid therapy was not sufficiently favorable to warrant the routine use of steroids in the treatment of ulcerative colitis. Although in the course of this therapy the temperature returns to normal, the patient feels more comfortable, and the appetite improves, the proctoscopic appearance of the rectal mucosa remains the same, the diarrhea usually is unaltered, and, when the drug is withdrawn, the fever frequently returns. Steroid therapy for ulcerative colitis should be used only in selected patients. Twenty units of corticotropin (ACTH) may be given intravenously daily when steroid therapy is instituted. This may be switched to Acthar Gel, 80 units administered intramuscularly daily, and subsequently to predisone or prednisolone, 15 to 30 mg. given by mouth daily.

In 60 of 106 patients subjected to surgical treatment up to 1949, the results were excellent; 17 of the 60 patients had ileostomy alone, 32 had colectomy after preliminary ileostomy, and 11 had other surgical procedures. Ten obtained reasonably satisfactory results, 11 were therapeutic failures, 8 were lost to follow-up, and 17 died within 2 months after the operation. Surgical treatment is indicated only for those patients who continue to be acutely or chronically ill despite an intensive trial on adequate medical treatment. Ileostomy alone seldom arrests the disease and is attended with a mortality rate of 23%. When surgical treatment is necessary, subtotal colectomy and ileostomy in one stage is a safe procedure associated with a low mortality and low morbidity and is the operation of choice. It was performed on 105 patients who were operated on between 1949 and 1957; only 4 of these patients died in the hospital, and 1 died after his discharge from the hospital.

Recurrent and Persistent Varicose Veins. H. Dodd. Postgrad. M. J. 34:73-76 (Feb.) 1958 [London].

Follow-up studies on more than 1,000 patients from 3 to 10 years after operations for varicose veins revealed that the author had obtained good results in 90% of the patients. Yet in the period from January, 1952, to June, 1957, over 400 procedures had to be performed for varicose veins that had recurred or persisted after operation. These patients returned with complaints of prominent veins, itching, pain, swelling, eczema, or ulceration of the leg. These conditions were caused by several factors, either singly or in combination: 1. The diagnosis was incorrect or incomplete. 2. The operation was wrong or inadequate. 3. New varices had developed. 4. Follow-up care was omitted. After discussing these 4 points, the author shows that the treatment of persistent or recurrent varicose veins is the same as that of the primary varicose veins. The sites of high-pressure leak or leaks from the deep veins into the superficial veins are exposed beneath the deep fascia, and the vessels are divided, if possible, flush at their entrance into the main vein. There are 5 common leaks of venous hypertension, and experience shows that several may coexist, although 1 or 2 are the usual finding. The saphenofemoral and saphenopopliteal junctions are the most common, and then follow the incompetent communicating veins above the ankle. There are the communicating veins passing into the femoral vein at Hunter's canal and into the popliteal vein around the knee joint. Defective veins perforating the tensor fasciae femoris and the hamstring muscles are comparatively rare.

Describing the operation for persistent varicosities of the long saphenous veins, the author says that an operation in the groin or popliteal space in the presence of the varicocele-like masses of thin-walled veins and scar tissue which develop after inadequate ligation may require 1 to 1½ hours. The principle followed is that of approaching the femoral or popliteal veins through virgin tissue and working up or down until the saphenofemoral or saphenopopliteal junctions are found. These are transfixed with fine thread and divided. Then the faulty saphenous trunk is exposed at the ankle, the stripper is passed along it, and the trunk is stripped out. Operations for persistent or recurrent varices at other sites are also briefly described. Full diagnosis and adequate operations of recurrent varicose veins are exacting but satisfying. Many persons, who are otherwise well, are incapacitated by varicose veins, the commonest surgical condition. Most persons, including the aged, can be materially improved, if not cured, by good treatment.

General Principles of Fracture Management in the Aged. E. D. Bick. Surg. Gynec. & Obst. *106*:343-346 (March) 1958 [Chicago].

A series of more than 500 fractures and dislocations occurring among the elderly was studied. Tabulation of data on 516 persons, over the age of years, who sustained fracture and dislocations ws that, with 3 exceptions, the distribution is more or less the same as would be found in any group of adults. The exceptions are the hip, the vertebra, and the shoulder, which together represent 58% of the total. Fractures about the wrist, which are third in numerical order, would be equally high or higher in any general list. These represent another 14%. The 3 exceptions also represent temporary total disabilities, and 2 of them, the hip and the vertebra, often represent permanent partial disabilities of significant degree. Fractures occur more frequently in women than in men. In those between the ages of 60 and 75 years the ratio of females to males is 3 to 1; in individuals more than 75 years old the ratio is 11 to 1. The aged population of New York in 1956 showed an over-all ratio of 1.2 females to 1 male. One must therefore assume that elderly women are far more subject to fracture than are their male contemporaries.

There are no techniques especially applicable to the treatment of fractures of the aged, but there are limitations of objectives. First, there is a greater need for a resting period between emergency care and definitive treatment. Manipulation or surgery is best performed after the patient has been allowed time for recovery from the shock of trauma. A second limitation is the relative softness or compressibility of the bones. Aging bone will not withstand the internal pressures of screws, plates, or nails as readily as does more viable bone. This is, of course, a variable factor and does not necessarily contraindicate the use of internal fixation. However, such procedures are less dependable in the aged. A third limitation appears during the period of after-care. There is the normally decreased elasticity of the muscular and periarticular connective tissues. It implies easy postfracture strain of inelastic ligaments, capsules, and fascial planes. It becomes necessary, therefore, to temper the urge for early and rapid mobilization of the part by measures which to the tissues of an elderly person may cause excessive stretch. Enthusiastic attempts at exercise or self-stretching of the area may result in a pain-spasm sequence which retards rather than enhances mobility.

Recovery of reasonable mobility in shoulder fractures takes a much longer time than is generally anticipated. Attempts to accelerate the process by active exercise not only are apt to retard motion but also cause an unnecessary persistence of pain. In dealing with fractures of the vertebrae, graded daily walks are apt to be more salubrious than exercises directed to the muscles of the trunk. The demand of early "out of bed" is, of course, incontrovertible when its purpose is gained. However, too often the order is obeyed to the patient's actual detriment. To be lifted out of the freedom of a roomy and adjustable hospital bed and then to be immobilized in a sitting position by the cautious blanketing of a solicitous attendant who fears more the pneumonia of a draft than the hypostasis of bed is indeed a gross disservice.

PEDIATRICS

Severe Staphylococcal Infections in Young Children: The Isolation of Micrococcus Pyogenes Var. Aureus with a Specific Bacteriophage Pattern. M. L. Cooper and H. M. Keller. A. M. A. J. Dis. Child. 95:245-252 (March) 1958 [Chicago].

During the 4th week of June, 1956, strains of coagulase-positive hemolytic Staphylococcus pyogenes var. aureus with the bacteriophage pattern 42B/44A/47C/52/80/81, apparently highly virulent for infants, were isolated from 7 patients admitted to the Children's Hospital in Cincinnati. Six of these patients were critically ill, 4 with pneumonia and empyema, 1 with pneumonia and a large deep intramuscular abscess, and 1 with pneumonia. The 7th infant was seriously ill with a large abscess. In *the course of a year a total of 77 persons, including* 67 patients and 10 asymptomatic carriers, were found to harbor staphylococci with the same bacteriophage pattern. Among the 67 patients there were 60 children with skin pustules, abscesses, pneumonia, empyema, pharyngitis, bronchitis, pyarthrosis, acute otitis media, and vaginitis and 7 adults with abscesses. The 7 adult patients with abscesses included 2 nurses on the infants' ward, 2 technicians in the bacteriology laboratory, and 3 parents whose children had acute staphylococcic infections. Among the 10 asymptomatic contact carriers were 3 siblings of patients, 2 children of patients, 1 student nurse, 2 nurses' aides, and 2 physicians. In vitro sensitivity tests showed that the staphylococci were sensitive to bacitracin, chloramphenicol (Chloromycetin), erythromycin, and novobiocin; they were resistant to chlortetracycline (Aureomycin) and dihydrostreptomycin and, with few exceptions, to penicillin and tetracycline.

Three months after the first patient was admitted to the Children's Hospital nasopharyngeal cultures of 117 personnel on the infants' ward revealed that 3 were harboring coagulase-positive hemolytic Staph. pyogenes var. aureus with the bacteriophage pattern 42B/44A/47C/52/80/81. These staphylococci were readily transmitted to other members of the families of patients. A study of 14 families revealed the presence of these particular staphylococci in 27 of a total of 53 persons. In 3 of these families, all 13 members were shown to be harboring these staphylococci—in abscesses in 5, in empyema fluid in 3, and in the nasopharynx in 5 asymptomatic carriers. Of the 42 infants under 1 year of age, 28 had a common place of birth, and 25 of the 28 infants were born in May, June, or July, 1956. A survey of that institution revealed the presence of infants and mothers with pyogenic infections from which strains of Staph. pyogenes var. aureus were isolated with the bacteriophage pattern 42B/44A/47C/52/80/81. Therapy consisted of the administration of 1 or more antibiotics to which the Staphylococcus organisms were sensitive in in vitro tests. Good clinical results were usually obtained with chloramphenicol, erythromycin (Ilotycin), and novobiocin (Albamycin). There were 2 deaths among the infant patients.

Neonatal Osteomyelitis: A Disease Different from Osteomyelitis of Older Children. A. M. Clarke. M. J. Australia 1:237-239 (Feb. 22) 1958 [Sydney].

Neonatal osteomyelitis differs so much from acute hematogenous osteomyelitis of older children that it is virtually a different disease. Analyzing 24 cases that occurred during the past 5 years at the Royal Children's Hospital, Melbourne, the author found that the bones involved were as follows: femur, 8 cases; maxilla, 6; humerus, 5; vertebra, 3; clavicle, 2; ulna, 2; radius, 1; tibia, 1; talus, 1; and phalanx, 1. *Several bones were involved in 3 cases, and there* was 1 death from the severe pyemic type of infection. Only 3 patients had involvement of the upper end of the femur and the hip joint. The possibility of primary involvement of a vertebra is also demonstrated by 3 cases. These were not discovered until large retroperitoneal abscesses had developed. The clinical course of neonatal osteomyelitis contrasts with that of osteomyelitis in older children in that there is often little or no toxemia or pyrexia and little systemic disturbance.

Blood culture often gives negative results. Abscess formation and joint involvement are common. Sequestra are rare. A marked feature is the tremendous amount of irregularly shaped extracortical new bone formation, the extent of which is determined by the subperiosteal abscess. Bone destruction and widening of a joint space may be obvious. There are 2 different forms of the disease. In a minority of infants, in whom it is an incident in septicemia, the condition is fatal, whereas in the majority of infants, the constitutional disturbance is not great, and the condition might be called benign except for the crippling deformities which can result. Pus for culture was obtained in the majority of infants, and Staphylococcus aureus was grown on every occasion. The suggested pathogenesis is that an infected thrombus, often originating in the umbilicus, lodges in the vascular network of the metaphysis of a long bone; but as the newborn infant has little cortical bone, it, together with the cancellous bone, is soon penetrated, and pus escapes into the subperiosteal area and ruptures into the soft tissues. The periosteum in infants strips up easily, so that there is not much pus under pressure to cut off the blood supply of the shaft. Consequently, an extensive involucrum is formed, but sequestration of dead bone is uncommon. Pus escapes into the soft tissues: this saves the cortex from the destruction noticed in older children.

Whatever the local manifestation, there are often associated paronychia, skin pustules, or cord infection derived probably from 1 of the following sources: prenatal intrauterine infection; infected liquor amnii after rupture of the membranes; maternal vaginal organisms; fingers and apparatus used in cleansing the baby's mouth after birth; the mother's skin, nipples, or milk; and the skin, nose, or upper part of the respiratory tract of nurse or attendants, the last-named being by far the most important. Osteomyelitis of the maxilla is relatively common (6 cases in the present series of 24). In none of the cases was the diagnosis made before pus was exuding from sinuses inside the mouth. Usually the first sign that something is amiss is that a swelling is seen in a cheek, the infraorbital area, or an eyelid. Exophthalmos or conjunctivitis may cause the patient to be directed first to an ophthalmologist. An alveolar swelling sometimes comes first and may proceed to perforation and discharge. Premature eruption of teeth is a characteristic phenomenon. This acceleration of eruption is probably due to increased vascularity in response to infection. Pus discharging from 1 nostril may result in an incorrect diagnosis of dacryocystitis. Successful treatment depends on early diagnosis, adequate chemotherapy, and prevention of dislocation or deformity. Early diagnosis depends on the condition's being suspected and on the appreciation of early signs, such as local edema or refusal to move a limb. In order to keep ahead of the drug-resisting characteristics of the infecting organism, the latest antibiotic should be used in adequate dosage and for sufficient time, 3 weeks being a minimum. Affected limbs should be immobilized early in their optimum position. This is of supreme importance in the hip.

Management of Nocturnal Enuresis in Childhood. S. J. McClendon. Arch. Pediat. 75:101-105 (March) 1958 [New York].

The author treated 32 boys and 28 girls, between the ages of 8 and 14 years, for nocturnal enuresis with meprobamate. The patients were selected because of the failure of all other measures ordinarily employed in the treatment of this condition. In all patients, organic diseases and anomalies of the bladder or urinary tract had been excluded by careful history, physical examination, catheterized urine specimens, or complete urologic studies including retrograde pyelograms and cystoscopic examinations. Complete neurological examinations were done on all, including roentgenograms of the lower spine and sacrum to exclude neurological disease, spina bifida, and congenital anomalies. Instructions were given concerning voluntary bladder training, fluid restriction after 5 p. m., avoidance of harsh disciplinary measures, and electric timing devices. These measures were discussed at a conference with both parents. The child in each case was given specific instructions about these things and also was given encouragement about the final outcome of the enuresis. The initial dose of meprobamate was 400 mg. given at 6 p. m. After one week, if there had been no improvement, the dose was increased to 800 mg. given in 2 divided doses at 4 p. m. and 8 p. m. This dosage was maintained for 30 days irrespective of results. If a success was secured, the dose was reduced to 400 mg. given at 6 p. m. After 30 additional days of treatment, administration of the drug was discontinued entirely. Each patient was followed for 6 months after withdrawal of the drug. If relapse occurred, retreatment for 1 month was again advised.

Of the 60 patients, 41 obtained a complete success, 10 obtained a partial success, and 9 were therapeutic failures. Complete blood counts and routine urinalyses made every 2 weeks revealed that there were no disturbances in either category. No side-effects of the drug were noted. The use of meprobamate is not suggested as complete relief for enuresis. However, the high percentage of children who were benefited from the drug makes meprobamate in the dosage described worthy of a trial in those patients with noctural enuresis, who are free from bladder or kidney disease or anomalies, when all other measures of management have failed.

UROLOGY

Needle Biopsy of the Kidney. A. W. Bohne, R. C. Ackles, D. R. Drew and K. L. Urwiller. J. Urol. 79:393-396 (March) 1958 [Baltimore].

The authors describe their technique of needle biopsy of the kidney, which they used during the last 18 months in 30 biopsies. They obtained renal tissue in 23 (76%) of the 30 patients, and they show that their results compare favorably with the results obtained by others. There were few complications. While all the patients had microscopic hematuria, gross hematuria was observed in 3 of the patients, but there was no instance of retroperitoneal hemorrhage. Complications which have been reported or anticipated included retroperitoneal hemorrhage, perforation of an intra-abdominal viscus, dissemination of a malignant or tuberculous process, or perirenal infection. The authors believe that the patient should be hospitalized for this procedure, mainly for adequate postbiopsy follow-up. It is a relatively safe procedure if done with adequate knowledge of renal position and realization of possible complications. Needle biopsy of the kidney can either correct or confirm clinical impressions.

Urological Complications of Stromal Endometriosis. C. A. Macfarlane, C. V. Hodges, H. V. Anderson and R. C. Benson. J. Urol. 79:436-446 (March) 1958 [Baltimore].

Stromal endometriosis is a type of primary uterine neoplasm whose infiltrative growth into the parametrial areas secondarily involves other pelvic viscera. Most authors agree that the basic origin of this neoplasm is from endometrial tissue or its embryonic precursor. The one opposing concept is that of Pedowitz, who believes that this neoplasm has its origin in vascular tissue and has, therefore, classified this tumor as a hemangiopericytoma. Stromal endometriosis generally occurs during the second half of the reproductive life. The presenting complaints include those of menometrorrhagia, abnormal noncyclic uterine hemorrhage, postmenopausal vaginal bleeding, pelvic pain, and lower abdominal tumefaction. The one most constant physical finding on examination is that of a symmetrically enlarged uterus. This neoplasm is distinguishable from adenomyosis and ectopic endometriosis. In the enlarged uterus diffuse infiltration of the the myometrium is evident as cord-like masses. Neoplastic growth near the endometrial surface produces an intrauterine polypoid growth in about 45% of these tumors.

With involvement of the urinary bladder, adnexa, intestine, and peritoneum, multiple firm nodules of a yellowish color are usually seen on the serosal surface. Cyst formation is not infrequent and occurs with infiltration of ovarian tissue. The tendency of stromal endometriosis to infiltrate in and along lymphatic and vascular channels has led to surgical resections that are either inadequate or deliberately palliative. The tumor residuum remaining in the parametrial areas or in the cervix after subtotal hysterectomy infiltrates the tissues and organs of the pelvis. The morbidity and mortality of stromal endometriosis are a function of involvement of anatomically vital sites rather than of neoplasm per se. Involvement of the urinary tract has been reported as approximately 12% of all cases reviewed.

In the 57-year-old woman, whose history is presented, the presenting complaints were those of an increasingly protuberant abdomen and edema of the left leg. The most striking feature on physical examination was a rounded, smooth, firm, intra-abdominal mass which extended 24 cm. above the symphysis pubis. This mass had invaded the entire pelvis, and there was a solid nodular invasion of the anterior vaginal wall. The bladder would not expand sufficiently to allow satisfactory cystoscopic examination. An exploratory laparotomy revealed that a large left ovarian cyst had 1 area of solid tumor within its wall. The peritoneal cavity itself was free of neoplastic infiltration, and there was no encroachment upon the sigmoid colon. Tumor had involved both parametrial areas with extension to, but not into, the pelvic musculature on the right. The anterior vaginal wall and vesical floor were grossly thickened. Tumor was also palpable within the dome and fundal areas of the bladder wall itself, and a yellowish subserosal nodule of tissue was present on the bladder fundus. The right ovary was replaced by a solid tumor mass. The downward course of both ureters ended in solid neoplasm with marked dilatation on the left. Anterior pelvic exenteration was performed, and urinary diversion was accomplished by means of bilateral ureteral transplants into an isolated ileal conduit with a cutaneous ileostomy. The surgical specimen weighed 715 Gm. minus the fluid contents of the ovarian cyst. Identified in the neoplastic mass were the urinary bladder, the distal portions of the ureters, urethra, a greater portion of the vagina, and both ovarian masses. This case history illustrates the usual characteristics of this disease and the surgical role of the urologist in relation to its treatment. Stress has been placed on palliative urinary diversion and curative surgical extirpation.

Malignant Pheochromocytoma with Voluntary Ability to Elevate Blood Pressure. C. L. Ransom, R. R. Landes and C. G. Gaddy. J. Urol. 79:368-376 (March) 1958 [Baltimore].

The authors present the history of a 37-year-old man who on the day of admission to the hospital, because of a strange feeling in his chest and a sense of suffusion throughout his face when bending over or flexing himself laterally, had come directly from work to his physician. At this time, the blood pressure was 230/110 mm. Hg. When the blood pressure returned to normal, it could again be elevated at will by the patient with lateral flexion of his trunk, but direct palpation did not reproduce the phenomenon. Intravenous pyelograms demonstrated a mass lying superior to the left kidney with distortion of the renal calyceal and pelvic structures. At operation the kidney was found to be involved in a large globular mass about the size of a football. Despite generous exposure, only about the lower third of the neoplasm could be removed. The renal pedicle and the entire medial portion of the tumor appeared to be inextricably involved with the aorta and stomach in 1 amorphous mass. Since removal was impossible, the incision was closed. The patient died 14 hours after the operation as the result of a severe hemorrhage rather than of interference with the pheochromocytoma. Microscopic studies corroborated the malignant character of the pheochromocytoma, although frozen sections from the tumor capsule during the operation had been reported as neuroblastoma.

The authors cite literature on malignant pheochromocytoma, pointing out that in large series of cases of pheochromocytoma the incidence of malignancy usually ranges from 8 to 11% but that in bilateral pheochromocytomas it reaches 30%. Pressor effects, either sustained or paroxysmal, may or may not be present in malignant pheochromocytoma. The diagnosis of malignancy should be based not on cellular pathology alone but rather on evidence of invasion or metastasis. Pheochromocytomas which are diagnosed as benign may later show metastases.

Solitary Adenoma of the Kidney. F. C. Bauer Jr., D. E. Murray and E. F. Hirsch. J. Urol. 79:377-382 (March) 1958 [Baltimore].

The authors present the history of a 65-year-old woman, who was first hospitalized in April, 1951, complaining of diffuse colicky pain in the abdomen for several months. The pain was sometimes relieved by a laxative. It became localized in the left side of the abdomen. The patient had had loose stools for several years; mucus was present but no blood. Roentgen-ray films of the abdomen disclosed that the right kidney was not enlarged and that the left was poorly visualized. Barium enema revealed diverticula of the rectosigmoid and the distal part of the colon. No erythrocytes were found in the urinary sediment. The patient was admitted again on Sept. 4, 1956, because of (abdominal) soreness and occasional sharp pain attributed to diverticulitis of the colon. There was a diffuse tenderness of the abdomen about the umbilicus, and an indefinite mass was palpated in the region of the left kidney. Roentgen-ray films revealed a large, soft, ovoid tissue mass in the left upper quadrant, which closely approximated the kidney shadow and displaced the colon to the left. A comparison with films taken during the previous hospital stay disclosed that the soft tissue mass on the left side was present previously and had increased only slightly in size. An intravenous pyelogram demonstrated a 12-by-14-cm. mass extending from the lower pole of the left kidney. The mass had faint densities (calcium), and the lower portion of the kidney was obscured or obliterated by the mass. The inferior calyces on the left were distorted laterally and medially and appeared to override the mass.

The left kidney was removed surgically. It had a solid tumor in the lower pole without extension into the renal vein or renal fossa. Histologically, the tumor consisted of solid cords of medium-sized cells with an abundant, finely acidophilic cytoplasm and small, oval nuclei. Although most cells were uniform in size, a few were large with multilobular nuclei. The symptoms disappeared after the operation, and the patient was still well 8 months later. Adenomas of the kidney occur as a solitary tumor of an otherwise normal kidney and as single or multiple tumors of an arteriosclerotic kidney. [illegible]ologically, adenomas are papillary, alveolar, or [illegible]ular. Adenomas of the arteriosclerotic kidney frequently are papillary. Alveolar adenomas are rare. Transitions from adenoma to carcinoma (hypernephroid) have been described.

Topical Anesthesia of the Vesical Mucosa as a Tool for the Management of the Neurogenic Bladder. E. Bors. J. Urol. 79:431-435 (March) 1958 [Baltimore].

The author studied the effect of topical anesthesia of the vesical mucosa in 124 patients with spinal cord lesions, of whom 112 had traumatic cord damage at various levels of the neuraxis below C-5, and 12 had nontraumatic diseases, such as mulitple lesions, combined degeneration, tabes, tumor, radiculitis, and partial aplasia of the sacrum. One hundred twenty-one patients had upper and 3 patients had lower motor neuron lesions. Prior to the instillation of 2 or 3 oz. of a 0.25% aqueous solution of Pontocaine, the residual urine and capacity of the bladder were determined. The Pontocaine remained in the bladder for 10 minutes and was then drained. Another residual-capacity test was done after 1 hour, and again after 24 hours. The type of voiding was observed, whether by reflex, extrinsic pressure (abdominal or manual), or a combination of both. The fluid intake was regulated by giving the patient 1 glass of water every hour during waking hours. Of a total of 124 patients, 35 responded so well to the procedure that they became catheter free; the results were good in 29 of the 112 patients with traumatic lesions and in 6 of the 12 with nontraumatic lesions. The effect of mucosal anesthesia was superior to that of sacral nerve anesthesia, which was, in turn, superior to that of pudendal anesthesia, in the 34 patients in whom all 3 methods were used.

Although the method was primarily devised for the treatment of patients with upper motor neuron lesions, it also benefited 2 patients with lower motor neuron lesions. It proved valuable in 7 of 25 patients with a preceding transurethral resection of the vesical neck, which alone did not establish bladder function. The fact that the 2 patients with lower motor neuron lesions responded favorably to topical anesthesia suggests that, in addition to the sacral mucosal reflex arcs, similar lumbar mucosal reflex arcs exist; impulses from the mucosal receptors would then be recruited by the lumbar spinal cord into an efferent outflow to the lissosphincter of the bladder. This problem needs further study, because, if correct, it would also extend the scope of the mechanism of Pontocaine action in cases with upper motor neuron lesions. Inasmuch as the sacral and lumbar afferents carry stimuli from mucosal receptors, it would seem likely that a combined relaxation of the lissosphincters and rhabdosphincters may result from this interruption of the afferent limbs of the reflex arcs. Thus, the numerically better effect which follows topical anesthesia can be understood in comparison with the other 2 methods of pudendal or sacral nerve anesthesia, which act only upon the sacral reflex arcs. Combinations of topical anesthesia with pudendal and sacral nerve anesthesia are proposed for future study.

OPHTHALMOLOGY

Lesions of the Lids: A Statistical Note. R. B. Welch and J. R. Duke. Am. J. Ophth. 45:415-416 (March) 1958 [Chicago].

The clinical and histopathological characteristics of 617 lid lesions, their distribution with respect to sex and age, the site of predilection, and the percentages of correct clinical diagnoses were studied at the Wilmer ophthalmic pathology laboratory of the Johns Hopkins University and Hospital between Jan. 1, 1952, and Dec. 31, 1956. Three hundred eight (50%) of these lesions were incorrectly diagnosed, illustrating the uncertainty of reliance on clinical impression alone. One hundred twenty-five (20.3%) of the 617 lesions were papillomas, 89 (14.4%) were nevi, and 80 (13%) were chalazia. Clinically, papilloma was correctly diagnosed in 70% of the cases. Seventy-four per cent of these lesions occurred in patients over 40 years of age. The occurrence of papilloma was equally divided between the sexes, and no site of predilection was manifest. Thirty-six per cent of nevi were correctly diagnosed clinically, and 80% of these lesions occurred in patients over 30 years of age. Of 85 patients with this type of lesion whose sex was known, 64 were women, suggesting a significantly higher incidence of this lesion in the female sex. No site of predilection was manifest. Chalazion was correctly diagnosed clinically in 70% of the cases; this lesion occurred with equal frequency in patients of all ages. No sex or site predilection was manifest.

Sixty-eight (11%) of the lesions were basal-cell carcinomas. This type of carcinoma occurred 8 times more frequently than either the squamous or the basosquamous carcinoma. Basal-cell carcinomas were correctly diagnosed clinically in 56% of the cases and were most often incorrectly called papillomas, nevi, recurrent chalazia, or cysts. When all types of carcinoma were grouped together, the 2 sexes were equally affected. Only 12.5% of the lesions occurred in patients less than 40 years of age. The highest incidence of occurrence (23%) was observed in patients in the 6th, 7th, and 8th decades. The lower lid was more commonly involved than either the upper lid or the canthus. Epidermoid, dermoid, epithelial, and sebaceous cysts grouped together accounted for 17.3% of the lesions. The percentage incidence of correct diagnoses ranged from 4% for the epidermoid cysts to 70% for the dermoid cysts. Aids in the diagnosis of dermoid cysts were factors of age and location. Sixty per cent of the dermoid cysts occurred in patients in the first decade of life, and 75% of them were on either the brow or the upper lid. Ninteen lesions were xanthelasmas, too few in number to warrant statistical consideration. However, all of these were correctly diagnosed clinically. Fourteen of the 19 lesions involved the upper lid.

The Management of Endophthalmitis Following Cataract Extraction. G. Pico. A. M. A. Arch. Ophth. 59:381-385 (March) 1958 [Chicago].

In the course of 740 cataract extractions carried out by the author between 1948 and 1956, endophthalmitis developed in 5 patients. The author states that this incidence of 0.65% is in accord with that in most other recently reported series. Only a limited number of cases are on record in which endophthalmitis complicating cataract extraction has been treated successfully. In 2 of the author's 5 patients with intraocular infection, managed, respectively in 1951 and 1952, the end-result was phthisis bulbi. In the light of present knowledge, it is clear that the dosages of penicillin and chloramphenicol employed were not adequate. With the advent of the newer antibiotics, the prognosis seems somewhat improved. Either chloramphenicol or tetracycline is the antibiotic of choice, since both have the ability to penetrate through the blood-aqueous barrier when they are given in massive dosages. Both have broad antibacterial spectrums, and both are effective when administered orally. The use of a corticosteroid with the antibiotic is recommended, as it will produce a rapid diminution of the inflammation and thus prevent the destruction of the retina and choroid.

In 2 of the 3 patients treated respectively in 1954, 1955, and 1956, the outcome was happier. In each instance treatment was instituted immediately after endophthalmitis appeared in the form of a vitreous abscess. Initial improvement was evident within 24 to 48 hours after therapy was begun, and in the course of 2 or 3 weeks the vitreous gradually cleared. The oral dosages of both the antibiotics and the corticosteroids were gradually diminished as the eye quieted down and vitreous clearing became evident. In the remaining patient treatment was along the same lines, but the final vision was limited to finger count, not, it was believed, because of the intraocular infection but because of a retinal detachment, which was probably related to loss of vitreous at operation.

Variability of Accommodation During Steady Fixation at Various Levels of Illuminance. M. Alpern. J. Optic. Soc. Am. 48:193-197 (March) 1958 [Lancaster, Pa.].

By means of a stigmatoscope imaged by an optometer arrangement, the variability of the dioptric power of the eye during steady fixation was measured for 4 practiced observers over a range of intensities from 2.5 to 3 log photons (trolands) of retinal illuminance in one-half logarithmic steps. Two different viewing conditions (constant-size and variable-size test letters) were studied, but no significant difference between them was obtained. There was almost a 4-fold decrease in the variability of 10 optometer settings as the intensity was increased over this range. There was a sharp transition at 1 photon, suggestive of a discontinuity between scotopic and photopic vision. These changes could be eliminated by cycloplegia of the fixating eye. Essentially the same results were obtained when the refraction of 1 eye was measured objectively with a coincidence optometer, while the other eye fixated the chart. This latter technique is, however, less valid at the lower intensities because of the tendency to fixate the measuring light of the optometer.

These observations show that the dioptric power of the human eye is changing continuously even during the steadiest of fixations. The fluctuations in accommodation will at a given moment produce a distribution of intensity slightly defocused from the optimum distribution. Whether the eye is defocused positively or negatively, the fluctuations of accommodation will constantly change the distribution of intensity in the retinal image. A theory is developed which accounts for the limits of fluctuation as a special example of intensity discrimination. This theory postulates that the limits of fluctuation are proportional to the critical value of the quotient obtained by dividing the intensity difference threshold by the intensity of retinal illuminance. This theory suggests a possible explanation for the response of the accommodation of the eye to the addition and removal of a minus lens, and thus leads to a hypothetical answer to the theoretical question, "What is the stimulus to accommodation?"

INDUSTRIAL MEDICINE

Physical Examinations for Executives. L. Wade. A. M. A. Arch. Indust. Health 17:175-179 (March) 1958 [Chicago].

What are the health factors to be considered in the placement of personnel? What evidences of health impairment should one seek in periodic medical checkups? So far as the author is concerned, answers to these questions are not available. If there are health hazards in the "executive" environment, then the so-called executive health examination is a legitimate part of occupational medicine. The health status of 2 groups of employees (176 men in each) was examined. The first group was labeled "management" or "executive" purely on the basis of personnel classification data. The second group, labeled "control," was chosen at random from the remaining employees on the basis of age alone. Each man was examined 2 or more times by 1 of 3 board-certified internists who work on a full-time basis in the medical department of an oil company. The extent of individual examinations was left to the discretion of the individual physicians. The following procedures were fairly routine: (1) a detailed history emphasizing the occupational and social factors; (2) a complete physical examination of the disrobed patient, including digital rectal examination; (3) red blood cell count, hemoglobin level, white blood cell count, sedimentation rate, and packed cell volume; (4) urine examination, including microscopic examination of the sediment; (5) stool examination for occult blood; (6) electrocardiogram; and (7) x-ray examination of the chest. Further examinations included gastrointestinal x-ray series and gallbladder series; proctoscopy and sigmoidoscopy, especially on men over 40 years of age or anyone having blood in the stool; ballistocardiography; exercise tolerance test; determinations of protein-bound iodine and blood cholesterol; and cystoscopy. These additional tests were chosen on the basis of the examining physician's findings in the more or less routine part of the examination.

A table that lists the diseases occurring in 10% or more of both groups of men shows that obesity existed in 30.9% of the executives and in 32% of the controls. For arthritis and rheumatism the executive and control percentages were, respectively, 21.2 and 11.2%; for hemorrhoids, 20 and 21.3%; for arteriosclerosis, 19.4 and 19.5%; for hypertensive disease, 19.4 and 18.9%; for anxiety states and neuroses, 19.4 and 13%; for back symptoms, 11.5 and 5.9%; and for hay fever, 10.3 and 11.2%. There was no clear-cut evidence that the working environment of management or executive personnel had any peculiar hazards. The author believes that, in the absence of such demonstrable hazards, it is unwise for the physician to be dogmatic regarding health factors in the selection of executives. Nor is it wise for the physician to narrow his health evaluation to any specific variety of disease process. Rheumatic complaints and disease were significantly more frequent in the executive or managerial group than in the control group. This will be investigated further.

Carbon Monoxide Asphyxia, a Common Clinical Entity. M. Katz. Canad. M. A. J. 78:182-186 (Feb. 1) 1958 [Toronto].

The author first presents the history of a garage mechanic who was hospitalized when he became unconscious while at work. When he recovered consciousness, he complained of loss of power of his hands, paresthesias in the extremities, blurring of vision, weakness, and dizziness. During the next 8 months he complained of 4 main symptoms: headache, anorexia, dyspepsia, and tiredness. In the absence of positive physical or laboratory findings, his trouble was considered psychosomatic. Because the illness recurred whenever the patient returned to work in the garage, carbon monoxide poisoning was suspected. Spectrographic examination of a blood sample revealed 18.5% carboxyhemoglobin. The patient was taken off work and given inhalations of carbogen, a mixture of oxygen (95%) and carbon dioxide (5%), 1 hour daily for a week. After the first treatment he noticed marked improvement, and he developed a hearty appetite. All symptoms disappeared.

The author observed 30 patients with carbon monoxide poisoning in the course of the last 3 years. Observations on these and on 11 others observed by members of his medical group are reviewed. It is pointed out that the diagnosis of carbon monoxide poisoning can be based on the following criteria: 1. The blood level of carboxyhemoglobin is 10% or more. 2. Symptoms of vague ill-health usually include 1 or more of such complaints as headache, anorexia, dyspepsia, weakness, and dizziness. 3. The symptoms should clear 4 to 7 days after removal from exposure and after daily inhalations of carbogen for 1 hour. (The addition of carbon dioxide to the mixture increases the respiratory rate and facilitates the dissociation of carboxyhemoglobin.) 4. No other medication is necessary. 5. The patient is symptom-free when the blood level of carboxyhemoglobin is reduced to below 10%.

The 41 patients fell into 3 environmental categories: (*a*) garage workers; (*b*) drivers of vehicles (trucks, tractors); and (*c*) housewives. Operators of farm tractors accounted for a large number of cases. Many diesel farm tractors have a vertical exhaust stack no higher than the driver's head. The driver may complain of headache and malaise after a prolonged period on the tractor. In enclosed vehicles the source may be a defective manifold or muffler. Housewives comprised 25% of the cases. Washing machines operated by gasoline engines caused illness in some. In 1 instance the use of a gas-heated iron produced toxic concentrations of carbon monoxide. A frequent offender has been a "space heater" type of oil stove located in the family living room. The toxicology of carbon monoxide is discussed, and it is pointed out that provincial laboratories in Canada are equipped to determine the carboxyhemoglobin content of the blood. Compensation boards will now accept claims for illness arising out of exposure to carbon monoxide on the job.

Skeletal Alterations in Patients with Decompression Illness. C. Garavaglia. Minerva med. 49:172-175 (Jan. 17) 1958 (In Italian) [Turin, Italy].

Liberated gas bubbles remain longer in the bone marrow than in other tissues in persons affected with decompression illness. Occlusion of the terminal arterioles of the bones causes aseptic necrosis. The author presents the roentgenologic findings of bone lesions in 2 patients with decompression illness. The first patient was a 30-year-old man who had been working in caissons for 10 years. After the 5th occupational year he has begun to have pain in the joints, accompanied by otorrhagia, vertigo, and paracusis. Roentgenologic findings showed pseudocystic epiphysial alterations in the head of the right humerus and in both heads of the femur. No articular lesions were detected. The other patient was a 52-year-old man who had worked in caissons for 26 years. The first symptoms of decompression illness appeared 6 years after he started work and consisted of acute manifestation of decompression with pain in the right leg and in both knees. Muscle and joint pains have recurred frequently, which induced the patient to leave this occupation. During the last working years the joint disease had intensified and the right leg became shorter, resulting in limping. The roentgen-ray picture showed an almost complete disappearance of the head of the femur. This bone state is similar to an outcome of Perthes' disease. Persistence of pseudocystic areolae in the remnants of the head of the femur is a definite differentiating feature of the presence of decompression illness from Perthes' disease.

Prognosis and Work Capacity After Cardiac Infarction. E. Iisalo, H. Kalliola, A. Kasanen and E. Linko. Nord. med. 59:264-267 (Feb. 13) 1958 (In Swedish) [Stockholm].

Of the patients with cardiac infarction treated in the medical clinic in Åbo from 1952 to 1956, 370 were discharged as convalescent. From 6 months to 5 years later, 242 patients were reexamined, 41 were lost to observation, and 87 had died. Of the 242 patients, 60.7% reported return to regular work, mostly from 3 to 6 months after discharge, and 39.3% were unable to work. Sixty-eight patients were readmitted because of certain or suspected recurrence of cardiac infarction; 31 of these belonged in the poor-risk group. Digitalis treatment after discharge in cases of cardiac insufficiency was often found to be unsatisfactory, pointing to the need of more effective supervision of after-treatment. Two-thirds of the patients whose electrocardiograms revealed persisting auricular fibrillation and two-thirds of those with persisting QS pattern in the unipolar chest leads considered themselves capable of work. Of the 87 patients who died, 60 were in the poor-risk group and 27 in the better group. All the deaths occurred within the first year after the infarction. The mortality increased with age. The patients in the poor-risk group who became able to work have, for the most part, done unexpectedly well, even in physically hard work.

THERAPEUTICS

Chlorpromazine Jaundice: The Effect of Continued Chlorpromazine Ingestion in the Presence of Chlorpromazine Jaundice. E. M. Schneider, C. Daugherty and J. K. DeVore. South. M. J. 51:287-291 (March) 1958 [Birmingham, Ala.].

It has been estimated that jaundice occurs in approximately 1% of all patients receiving chlorpromazine. This jaundice has the character of an intrahepatic obstructive lesion. Treatment is largely empirical, but it is generally accepted that, when jaundice appears, the drug must be withdrawn. The present report is based on a study of 4 patients in whom the administration of chlorpromazine was continued without change after the appearance of jaundice. All 4 patients were inmates of a state mental hospital; 3 were women and 1 a man. All 4 patients had been receiving chlorpromazine in dosages of 150 to 200 mg. per day for 25 to 39 days prior to the appearance of jaundice. In each instance, chlorpromazine was continued without change in dosage until all clinical and laboratory evidence of jaundice had disappeared. On 3 of the 4 subjects, laboratory studies and biopsies of liver specimens were obtained within 3 to 5 days of the appearance of jaundice. In patient 2 there was a 12-day interval between the onset of icterus and the initial laboratory study. A liver biopsy attempt on this patient was unsuccessful. A second series of liver function tests was obtained on all patients 10 to 21 days after the initial observations. A third battery of hepatic function tests, together with liver biopsies on all subjects except patient 2, was performed 42 to 68 days later and was the final study on subjects 2, 3, and 4. Patient 1 was subjected to 1 additional series of liver function tests 151 days after the onset of jaundice.

Elevations of serum alkaline phosphatase and serum bilirubin levels were noted in all subjects initially. The bilirubin levels tended to return to normal somewhat earlier than did the alkaline phosphatase levels. In all patients serum lipid phosphorus determinations were higher during jaundice than after recovery. Liver biopsies were available on 3 of the 4 subjects during and again after clearing of jaundice. Bile canalicular plugging and periportal infiltration were noted in 2 subjects on the first biopsy but were normal on repeat examination. The third subject showed only some fatty change in both biopsies. In the present group of patients chlorpromazine therapy was continued with impunity after the appearance of chlorpromazine jaundice. The possibility of chlorpromazine inducing changes in bile viscosity or composition and in biliary sphincter tone was neither supported nor refuted by this study. However, the available data do cast doubt on the likelihood of chlorpromazine jaundice being due to hepatotoxicity or chlorpromazine sensitivity or to existing hepatic disease.

Cytostatic Medicaments and Malignant Tumors: *Clinical Results of Trials Carried On for Four Years.* A. Ravina and M. Pestel. Presse méd. 66:313-314 (Feb. 22) 1958 (In French) [Paris].

The records of 120 patients treated with cytostatic preparations for various types of cancer show that the actinomycins C and D are, on the whole, the easiest to manage. Hemorrhagic complications have been reported but are generally believed to occur less often than with most other cytostatics, especially nitrogen mustard. The other manifestations of intolerance, which consist chiefly of irritation of the digestive mucosa with stomatitis, anorexia, nausea, abdominal pain and diarrhea, and more or less extensive alopecia, are always transitory and comparatively easy to control or avoid. The best results were obtained in patients with lymphatic disorders, such as chronic leukemia or Hodgkin's disease, but in certain patients with other malignant conditions the actinomycins also proved beneficial, checking the malignant process and assuring survivals that were sometimes prolonged.

R 261 (N-desacetylthio-colchicine), a synthetic sulfurated derivative of colchicine, with greater antimitotic power and less toxicity than colchicine, was given intravenously to 20 patients. Several failed to show any improvement; in 2 who had bronchial cancers the tumor seemed to regress, but the treatment had to be discontinued because of the intense leukopenia to which it gave rise; and in a few others the progress of the disease was checked for periods of varying length. R 261 in a 2.5% pomade may also be applied topically to superficial or cutaneous cancers, either primary or metastatic, whether or not they are ulcerated. The potency of the drug, however, makes it hard to manage and in 2 of the authors' patients it led to shallow but extensive ulcerations that pursued a torpid course. An interesting point that should be further investigated is the fact that R 261 is capable of causing paroxysmal pain in the tumor and also in its metastases, the existence of which was sometimes revealed by this means. Similar focal pains have been noted, but very rarely, after the administration of actinomycin or E 39 (5-amino-7-hydroxy-imine 2,5-depropyloxy-3-6-benzoquinone), another cytostatic now being studied by the authors.

Azan (8-azaguanidine, sodium 5-amino-7-hydroxy-triazolopyrimidine) may inhibit the growth of certain cancer cells by acting on the purine metabolism. Well-defined regression of the functional and general symptoms, obtained by its use in a few patients, was never accompanied by any appreciable change in the size of the tumor. The number of patients who were given azan for malignant lymphatic conditions, for which the drug is chiefly indicated, was, however, very small.

Exophthalmos of Graves' Disease: A Summary of the Present Status of Therapy. E. P. McCullagh, M. Clamen, W. J. Gardner and others. Ann. Int. Med. 48:445-470 (March) 1958 [Lancaster, Pa.].

The authors report on 39 patients with exophthalmos of toxic diffuse goiter (Graves's disease), 20 of whom were treated with L-triiodothyronine, 10 were treated with both corticotropin (ACTH) and hydrocortisone, and 9 were subjected to pituitary surgery in an attempt to reduce extremely severe exophthalmos. Of the 20 patients with progressive exophthalmos treated with L-triiodothyronine for periods ranging from 2 to 11 months, the proptosis was reduced by 2 mm. or more in 9 patients, remained stationary in 9, and became worse in 2. The aim was to give L-triiodothyronine in the largest dose that the patient could tolerate with comfort, usually 100 mcg. per day (range, 75 to 200 mcg. per day). Six of the 9 patients showing significant recession did so at their first visit, 2 months after treatment was started. Each of the 10 patients treated with both ACTH and hydrocortisone received 50 mg. of ACTH intravenously for a period of 6 hours daily for from 5 to 16 days, and 200 mg. of hydrocortisone orally daily; the dose of the latter drug was reduced over a period of weeks. Duration of follow-up ranged from 1 to 4 months. There was symptomatic improvement in all 10 patients. The sense of conjunctival irritation, lacrimation, and any ocular pain that had been present usually diminished greatly or disappeared in from 1 to 3 days after treatment was instituted. Conjunctival and lid swelling apparently diminished in all but 1 patient. There was dramatic improvement in the proptosis as well as in the soft tissue swelling in only 2 of the 10 patients; active hyperthyroidism was present in these 2 patients.

Of the 9 patients subjected to pituitary surgery, 5 were operated on before 1946 and 4 were operated on since 1953 when adequate replacement therapy for severe pituitary failure had become available. The surgical procedures in these 9 patients included some combination of section of the pituitary stalk, cauterization of the anterior lobe, and placement of an impervious diaphragm of plastic, waxed paper, or tantalum above the sella turcica in the hope of interfering with regeneration of the "portal circulation" of the pituitary. In all 9 patients the exophthalmos improved postoperatively; in some it disappeared entirely, and visual acuity that had been extremely poor returned to normal.

The measures employed in the treatment of exophthalmos of toxic diffuse goiter should be chosen with care, chiefly on the basis of the severity or type of ocular changes and the rate and degree of progression of the disease. Estrogens and androgens as pituitary inhibitors have been of little or no value in the treatment of exophthalmos. Roentgen-ray irradiation of the pituitary gland may also be considered to be of little value, since heavy doses of this therapy do not produce hypopituitarism. If exophthalmos is the first evidence of toxic diffuse goiter and hypometabolism exists with it, the administration of desiccated thyroid, of thyroxin, or L-triiodothyronine, in at least a physiological dose, is indicated. If exophthalmos is increasing in severity, it is advisable to give thyroid hormone in larger than physiological doses up to the amount that can be tolerated by the patient without undesirable side-effects. In patients having severe swelling of the lids and conjunctivas, the use of ACTH and cortisone may be valuable. It is considered important to limit the intake of sodium to 500 mg. per day and to add several grams of potassium to the daily intake while ACTH and cortisone are being used; the use of an ulcer regimen also is advisable, if large doses of these hormone preparations are used. In severe cases of exophthalmos not responding to other measures of treatment, pituitary surgery may be considered. Experience with this type of treatment to date is small but encouraging. In the event of extremely rapid progression of the disease, when loss of 1 or both eyes is seriously threatened, orbital decompression may become imperative.

Value of Aminopyrine. L. Cardon, O. H. Comess, T. A. Noble and M. M. Pomaranc. Ann. Int. Med. 48:616-634 (March) 1958 [Lancaster, Pa.].

The authors report on 3 men and 3 women, between the ages of 33 and 51 years, with various febrile diseases to illustrate the potent antipyretic effect of aminopyrine. Of the first 3 patients, 2 had prolonged intractable fever of unknown origin but most likely due to acute exacerbation of rheumatic fever, and 1 had periarteritis nodosa with spiking fever. Aminopyrine, in doses of 5 grains (0.32 Gm.) 3 times daily and 10 grains (0.65 Gm.) 4 times daily, was the only drug which controlled the fever and reversed the progressive downhill course of the disease after weeks of ineffective therapy with large doses of chemotherapeutic and antibiotic agents. In these 3 patients the action of aminopyrine simulated that of a specific drug and proved to be lifesaving. Granulocytopenia did not occur in these patients, although the drug was given continually for up to 5 months to 2 patients and intermittently for up to 2 years to 1 patient. A tendency to leukopenia in 1 patient was readily controlled by reduction in dosage. The 4th patient with ulcerative colitis, rheumatic heart disease, and mitral stenosis received 5 grains (0.32 Gm.) of aminopyrine 4 times daily, affording a dramatic respite from fever which was refractory to all other treatment, including antibiotics and corticotropin (ACTH) for 17 days. During this respite the patient recovered much weight and strength and was thereby in much better condition to withstand the operation for perforation of the colon which occurred later on. Persistent spiking fever subsided by lysis as a result of treatment with 5 grains (0.32 Gm.) of aminopyrine 4 times daily in the 5th patient with carcinoma of the head of the pancreas. The 6th patient also had carcinoma of the head of the pancreas, with metastasis to the liver, associated with persistent spiking fever which had been refractory to prolonged treatment with penicillin, chloremphenicol, oxytetracycline (Terramycin), and aspirin. The temperature was restored to normal by treatment with aminopyrine.

Aminopyrine is of value particularly in conditions not amenable to therapy with specific chemotherapeutic and antibiotic agents or in patients in whom these prove to be ineffective, in patients in whom other antipyretics are not tolerated or in whom they have failed, or in patients in whom it is not advisable to assume the risks of therapy with corticotropin and the corticosteroids or in whom these agents have failed. Aminopyrine is still a uniquely valuable and occasionally a lifesaving antipyretic which deserves a trial whenever fever is a significant feature of the clinical picture of the disease. The danger of granulocytopenia from the use of aminopyrine, although real, has been overemphasized and is no greater than from many other drugs in common use today. Aminopyrine has its place in therapeutics under well-controlled clinical conditions and under supervision of a physician, but its careless and indiscriminate use is to be condemned.

PATHOLOGY

Cryptic Cervical Nodal Metastases: A Pathologic Study of Possible Primary Sources. M. S. Comess, M. B. Dockerty, and O. H. Beahrs. Arizona Med. 15:87-95 (Feb.) 1958 [Phoenix].

The authors studied 1,189 patients with proved metastases to cervical lymph nodes, who were seen at the Mayo Clinic between 1945 and 1953. In 103 8.7%) of these patients, the primary source of arcinoma spreading to cervical lymph nodes could t be found at the initial investigation. Three pa- nts could not be traced. The remaining 100 pa- nts were subdivided into 3 groups: 1. A primary mor was discovered at some time subsequent to the original examination in 40 patients. 2. Forty-four patients died without evidence of the source of the metastasis. 3. Sixteen patients were living and had no further evidence of malignant disease. If careful history, minute physical examination, and appropriate endoscopic, roentgenologic, and hematological studies are unavailing, the source for the presumed metastasis may be considered occult. Surgical exposure and histological diagnosis are considered essential in the management of a cervical tumor, the nature of which is indeterminate after clinical study. Fresh frozen sections are of decided help when, as is frequently the case, a definitive diagnosis can be made immediately by this method. Indicated operative procedures may be immediately performed. The histopathological findings were often of help in locating a cryptic primary tumor, particularly 1 in the thyroid gland. The histological type and grade of the secondary lesion determine in large part the prognosis and management of the individual case. Metastases of high-grade squamous-cell carcinoma in the submaxillary and upper deep jugular chains were found to imply unexpectedly favorable prognosis. Long-term survival without further evidence of neoplastic disease after varying treatment was noted in about 33% of patients with such lesions. No adequate explanation of the source of these tumors is available.

A Statistical and Histological Survey of Metastatic Carcinoma in the Skeleton. P. C. Meyer. Brit. J. Cancer 11:509-518 (Dec.) 1957 [London].

The histological files of a London hospital, which contained records of 14,154 autopsies from 1946 to 1955, inclusive, revealed 320 cases with skeletal involvement by secondary carcinoma. During the same period surgical material was obtained from only 20 cases of metastatic carcinoma in bone; the latter are not included in the present study. Although the skeleton is not examined routinely in all cases, a standard technique is employed. An examination of the relevant parts of the skeleton is carried out if justified on clinical or radiologic grounds or if there is evidence of any bone lesion at autopsy. Care was taken to exclude examples of direct skeletal involvement by carcinoma. The site and nature, whether of compact lamellar or cancellous type, of each portion of bone examined histologically were noted, and a quantitative estimate of the degrees of resorption and new bone formation was carried out. It was found that changes involving different bones in the same patient were remarkably consistent. The 320 cases are tabulated according to the location of the primary tumor. The findings in 2 comparable series of cases investigated by other authors are shown in the same table. The primary tumor was found in the bronchus in 124 of the patients, in the breast in 56, in the prostate in 53, in the stomach in 33, in the intestine in 11, in the kidney in 10, in the liver and bile passages in 6, in the thyroid in 4, and in smaller numbers in pancreas, esophagus, and uterus.

The author regards the 33 cases secondary to gastric carcinoma as surprising, since ordinarily gastric carcinoma is not generally considered as a frequent source of skeletal metastases. The low figures for renal and thyroid carcinomas are of great interest and reflect the low incidence of these conditions in the general population. Osteoclastic erosion was the main factor in resorption of bone, but a direct osteolytic action was frequently exerted by the stromal cells of the tumor. In many instances resorption of bone appeared to be the result of direct pressure by masses of proliferating epithelial cells. *Osteosclerosis* was produced by the apposition of new bone on existing trabeculae and by the formation of new trabeculae as a result of metaplasia of marrow cells. A complete absence of bony reaction or only a slight reaction was frequently observed in patients with the oat-cell variety of bronchial carcinoma, while a relationship between osteosclerosis and a high degree of histological differentiation could be established in the case of mammary and prostatic carcinoma.

Muscle Involvement in Boeck's Sarcoid. S. L. Wallace, R. Lattes, J. P. Malia and C. Ragan. Ann. Int. Med. 48:497-511 (March) 1958 [Lancaster, Pa.].

Between 1946 and 1956, random muscle biopsies were done *for diagnostic reasons on 42 patients* with sarcoidosis at the Presbyterian Hospital of New York. The patients in this group showed a clinical picture compatible with sarcoidosis; 32 of them had, in addition, pathological proof of the diagnosis, and the remaining 10 had a positive reaction to the Kveim test in the absence of pathological evidence of the disease. None of the biopsy specimens were *taken from an area with objective* clinical abnormality. They were taken most commonly from the gastrocnemius muscle because of its greater accessibility, although biopsy specimens also were obtained from the deltoid, pectoralis major, sternocleidomastoid, and platysma muscles and from otherwise unidentified muscles of the neck.

Twenty-three of the 42 patients with sarcoidosis showed pathological changes compatible with this diagnosis on biopsy of tissue from skeletal muscle. Four patients had sensations of muscle pain or aching, and 2 of these had sarcoid granulomatous lesions on biopsy. Six patients had migratory poly*arthritis, and 5 of them had muscle biopsies show*ing sarcoid granulomatous lesions. Seventeen patients with sarcoid lesions in the muscle had no muscle or joint symptoms whatever. There was no consistent correlation between objective changes in the muscle and the presence of lesions. Six of 17 patients with 1 or 2 organs involved by sarcoidosis had a positive muscle biopsy; 17 of 25 patients with 3 or more organs or systems involved by sarcoidosis showed sarcoid granulomatous lesions on muscle biopsy. The wider the dissemination of the sarcoidosis, the more likely the muscle biopsy was to show sarcoid lesions. The sarcoid granuloma in muscle was similar to that in other tissues. One *patient had a granulomatous arteritis in the muscle* due to sarcoid. There was no relation between age, sex, or race of the patient and the presence or absence of sarcoid granulomatous lesions on biopsy. Because of sparsity of lesions, routine sectioning at multiple levels proved to be of great importance in discovering sarcoid lesions in muscle. Although sarcoid granuloma is not specific for sarcoidosis, the use of muscle biopsy is indicated as an aid in diagnosis of sarcoidosis, particularly if no other histological specimens are available for examination.

RADIOLOGY

Treatment of Carcinoma of the Breast with Roentgen Therapy Alone. V. Racugno and A. Angei. Rass. med. sarda 59:497-506 (Sept.-Oct.) 1957 (In Italian) [Cagliari, Italy].

Baclesse, in France, and Nuvoli, in Italy, contend *that roentgenotherapy can substitute for surgical* treatment in both operable and inoperable types of carcinoma of the breast. This opinion led the authors to use roentgenotherapy in 17 patients during the period between 1953 and 1956. Seven patients had inoperable neoplastic lesions, some with ulcerations and extensive regional metastases. The other patients had the operable type of tumor. Biopsy by aspiration was performed in 14 patients with nonulcerative type of carcinoma. Histological findings revealed the presence of adenocarcinoma. The radiation was delivered from a 180-kv. x-ray machine. The filtration was 0.25 mm. Cu plus 1.0 mm. Al; the focus-skin distance was 40-50 cm. The *treatment was carried out in 4 areas;* the breast was irradiated through 2 opposite sections, 1 medial and 1 lateral, at a total rate of about 5,000 r.

Of 7 patients with inoperable tumors, 4 died within a period of 8 months to 2 years after discontinuance of the roentgenotherapy. The primary neoplastic lesion and regional metastases disappeared in 2 patients, but they died from pleuropulmonary involvement of the opposite side. All 10 patients with tumors classed as operable are still alive with no recurrence or metastasis in a period of 1 to 3 years after discontinuance of roentgenotherapy. The primary tumor and regional metastases have disappeared completely only in a few patients; *in the others the lesions have been considerably* reduced in size. The systemic reaction to the therapy in all patients was mild; local reaction was marked, but it subsided after the termination of treatment. Small residual areas of epitheliosis were observed in 3 patients, but these disappeared after topical medication for a few months.

Roentgenotherapy for Fibromyoma of the Uterus. B. Vidal and G. Englaro. Minerva med. 49:98-104 (Jan. 13) 1958 (In Italian) [Turin, Italy].

Roentgenotherapy was given to 239 patients with fibromyoma of the uterus at the General Hospital at Udine during the last 25 years. One hundred forty-three women (62%) were in their 40's, and 53 women (23%) were in their 50's. Small-sized fibromyomas were present in 76 patients (33%), medium-sized ones in 105 (45%), large-sized ones in 44 (19%), and very large fibromyomas in 7 (3%). Large-sized tumors were prevalent in women over 60 years old and medium-sized tumors in all other age groups. Sixteen patients did not complain of hemorrhage. Surgical therapy was contraindicated in about one-fourth of the patients. Regression in the size of the tumor occurred mostly in a period between the 3rd and the 6th month of therapy. No recurrence of tumor was observed, which was partly due to the castration caused by the roentgenologic procedure. The radiation was delivered from a 180-kv. x-ray machine. The filtration was 0.5 mm. Cu plus 0.5 mm. Al; the focus-skin distance was 40 cm. Total surface dose varied between 1,000 and 1,200 r per area when 4 portals were employed and between 1,500 and 1,800 r per area when 2 portals were employed.

Almost complete regression of fibromyoma and complete subsidence of hemorrhage and of associated symptoms were observed in 122 patients (53%), partial regression of fibromyoma and complete subsidence of hemorrhage in 110 patients (47%), and insignificant or no regression of fibromyoma and complete subsidence of hemorrhage in 7 patients (3%). Contact was lost with 7 patients after termination of the treatment. The best results were obained in those instances in which roentgenotherapy has suppressed ovulation. Good results were also obtained in 28 women in menopause; among these there was almost total regression of tumor in 10, partial regression in 13, and insignificant or no regression in 5.

PUBLIC HEALTH

oridation of Public Water Supplies and Its Relation to Musculoskeletal Diseases. C. L. Steinberg, D. E. Gardner, F. A. Smith and H. C. Hodge. New England J. Med. 258:322-325 (Feb. 13) 1958 [Boston].

The authors estimated the fluoride content of ash in 18 various bone samples obtained at autopsy or through surgical intervention from 14 patients, 13 of whom had various forms of arthritis, 1 of whom did not have arthritis, but all of whom had ingested fluoridated water for a period ranging from 3 years and 5 months to 4 years and 7 months. No excessively high concentration of fluoride was found in any of these specimens. Fifteen various bone samples obtained from 11 patients with various forms of arthritis and from 2 patients who did not have arthritis, all of whom were residents of a nonfluoridated water area, were analyzed for fluoride content expressed in parts per million of ash. The fluoride concentration value in bone of the residents of the area in which the water was not fluoridated and that of the residents in the fluoridated water areas were not statistically different. A careful review of the roentgenograms of both these groups, along with the bone fluoride content studies, failed to reveal any relation between various forms of arthritis and the ingestion of fluoridated water as recommended by health authorities.

The Risk of Ascaris Infestation From the Use of Human Sludge as Lawn Fertilizer. J. O. Bond. J. Florida M. A. 44:964-967 (March) 1958 [Jacksonville].

The modern sewage treatment process does not necessarily completely destroy all pathogenic organisms. An example is the municipal sewage disposal plant in Tampa which sells sludge to a local nurseryman who, in turn, retails it as lawn fertilizer. During the summer this arrangement was initiated, a local pediatrician treated a child with severe ascariasis and, in a careful history, obtained the information that the child had had contact with a lawn fertilizer obtained from this source. This paper is a report on the subsequent investigation to determine whether this sewage sludge was a source of infection due to Ascaris organisms in this community. Specimens of sludge were obtained at approximately biweekly intervals from the Tampa Municipal Sewage Disposal Plant, where sludge is removed from the settling basins, allowed to digest at 26.6 to 32.2 C (80 to 90 F) for approximately 30 days, and distributed to beds for drying up to 21 days. After determination of moisture content, the specimens were examined for Ascaris ova by the standard zinc flotation method and by quantitative Stoll counts. Three specimens each were taken from the raw, the digested, and the drying sludge. Dried sludge was the only source of plain commercial sludge for lawn fertilizer. Viable Ascaris ova in the range of 100 per milliliter were shown to be present in sewage sludge sold as lawn fertilizer in Tampa.

The second part of the investigation was to determine whether the children exposed to sewage sludge used as lawn fertilizer were actually infected by the ova known to be present. Two groups of children, who were alike in all respects except exposure to the fertilizer, were studied for prevalence of infection due to Ascaris organisms. No significant difference was found in the prevalence of the infection in these two groups of children, so that the sewage sludge used as lawn fertilizer was a potential, but not an actual, source of ascariasis in this community. Heat sterilization of the sludge for a minimum of 3 minutes at 65 C (149 F) would eliminate this potential hazard.

BOOK REVIEWS

Foundations of Neuropsychiatry. By Stanley Cobb, A.B., M.D., Sc.D. Sixth edition of work formerly known as A Preface to Nervous Disease. Cloth. $5. Pp. 313, with 16 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1958.

This authoritative book is small and easy to read. It contains an immense number of facts organized into a clear pattern, and the whole work is illuminated by the understanding that the author brings to his subject. The artificial barriers between neuropathology, neurophysiology, neurology, and psychiatry do not trouble him; he hurdles them easily and manages to achieve a satisfying synthesis of the classical anatomic point of view and the most modern functional concepts. The nonexpert should find this book useful either as an introduction or as a review. It touches on almost everything that has been thought and said about the central nervous system—makes it live and gives it meaning. The expert will be fascinated by the author's insight, his reasonableness, the skill with which he writes, and his mastery of his material. In a few places the expert may disagree with the author, but he will be interested to find the cause for the disagreement. The author is such a knowledgeable person that if the truth escapes him it is indeed elusive.

Chapters 1 through 5 show how the nervous system is built of simpler structures and how complex functions are organized. These chapters include much factual material on the autonomic nervous system, the localization of function in the brain, and relevant neuroanatomy. The author is at his best in chapter 6, where he argues in favor of abandoning the dichotomy, organic versus functional, which encumbers our thinking and seriously impairs an understanding of the brain. He propounds the advantages of a holistic approach in a way that is both interesting and convincing. The broad and inclusive frame of reference he recommends permits a complete statement of what the brain is and does. A narrower frame of reference would leave out much that is essential and show only a partial and distorted picture. Subsequent chapters deal with cerebral circulation, cerebrospinal fluid, disease states, psychological concepts, and psychopathological reactions. Neurochemistry is touched on rather lightly. This is unfortunate, because the basic unity of structure and function which the author sees so clearly is most evident when the brain is viewed on a molecular or submolecular level. At this level, structure and function are one and the holism for which the author argues is not a philosophical concept but a fact. If this book does not deal as extensively with brain chemistry as some might wish, it goes about as deep as is practicable for anyone who wishes to keep his feet on the ground of present-day neurology and view the peaks of psychological psychiatry. In the next edition, there will doubtless be longer sections on brain chemistry, for this is an area of knowledge that is growing rapidly. The brain can be compared to a telephone exchange, a calculating machine, a constellation of psychological constructs; but it is primarily a chemical organ.

Adventures in Medical Education: A Personal Narrative of the Great Advance in American Medicine. By G. Canby Robinson, M.D., LL.D., Sc.D. Cloth. $5. Pp. 338, with illustrations. Published for Commonwealth Fund by Harvard University Press, Cambridge 38, Mass., 1957.

This is the autobiography of a man whose career interests were in academic medicine at the time in which medical education was rapidly changing. The author began his medical study at the Johns Hopkins Medical School in 1899 as one of the 50 students in that institution's seventh class. This new medical school and its talented faculty, which were destined to exert a major influence on medical education in the United States, is pictured as seen by students in its early and formative days. The author believes that "the medical school had the social and intellectual spirit of a true university graduate school. Students were treated as mature men and women, and the teaching staff helped them to get the best medical education that each was capable of acquiring largely through his own efforts." His description of the course of study and the relationships of faculty and students represents an educational program and environment that, by contrast, clearly places the educational activities of many medical schools today at the undergraduate rather than at the graduate level. After some initial disappointments, described with refreshing candor,

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

CASTRATION AND MENTAL RETARDATION

To the Editor:—*Recently a sex problem has been encountered in a mentally retarded, 37-year-old man. At the age of 10 years this individual was examined at the Stanford-Lane Clinic and was given an IQ rating of 5½ years. He attended a rural school for eight years but made little progress and is at present unable to read and write. From external observation, he appears to be a normal, healthy, adult male, well built, well mannered, and well behaved. A casual observer would suspect nothing abnormal unless he tried to engage the man in conversation. Recently the parents have become quite concerned because of the advances being made by their son toward small female children of neighbors and relatives who occasionally visit. They realize the legal and psychological possibilities involved. They also realize that sterilization by vas ligation or medication is no answer. The extreme alternative of castration is being considered, since institutionalization of this individual would not be warranted. Please give advice on any other way to handle this problem.* *M.D., California.*

Answer.—The first question that comes to mind in such a situation is, "What is the clinical nature of the mental deficiency?" The result of the psychological examination at the age of 10 years really does not constitute a clinical diagnosis. As a first step in the formulation of a plan of action, a restudy of the patient by a physician experienced in the evaluation of mental retardation in adults is indicated. If the patient is as mentally retarded as the test in his childhood seems to indicate, it is quite possible that some of his sexual interests derive from simple sexual curiosity. A physician who has a good relationship with such a patient and who has some aptitude in conversing with mentally retarded individuals could provide him with sexual information and request him to return to talk about sexual matters and sex differences when he wishes. The neighborhood children do need protection, but some of this is the responsibility of the parents of the children and should not be expected to be entirely that of the retarded individual, although, curiously enough, it is this latter viewpoint that prevails in most communities. On occasion, such a handicapped individual is goaded or teased into sexual activity by hostile persons in his immediate environment. The sexual drive of a severely retarded individual is usually not great, so that it again becomes important to evaluate the nature and extent of the retardation at the patient's present age. Decision about castration should be influenced by the extent of the patient's sexual energies and drives and also by the cause of the retardation; for example, familial and, therefore, genetically transmitted mental deficiency would cause more consideration to be given to castration than would the presence of mental deficiency that derives from brain damage.

Answer.—Castration may well constitute mayhem, as defined in the penal code of the state. Regan, in his book, "Doctor and Patient and The Law" (St. Louis, C. V. Mosby Company, 1949), states that the California Penal Code, Section 203, defines mayhem as follows: "One who unlawfully and maliciously deprives another of a member of his body, or disfigures or disables it or renders it useless, etc., is guilty of mayhem."

CLEANING OF OPERATING ROOMS

To the Editor:—*Is it advisable to scrub the operating room floor between each surgical case, or is it sufficient to scrub the floor once a day and in between "dirty cases" only? A question has been raised as to whether mopping introduces more germs between operations than leaving the floors as they are. What is the policy in large teaching hospitals?*

R. P. Froeschle, M.D., Hazen, N. D.

Answer.—The floor is the principal reservoir for dust and bacteria that contaminate operating room air. The operating room floor must be cleaned and disinfected daily. All furniture must be removed to make the entire surface accessible. Trash is picked up with a vacuum cleaner. Shelving, mouldings, and lamps are wiped with a cloth dampened in a quaternary or phenolic germicide. A fresh solution of detergent germicide (quaternary, iodophorm, or phenolic) is made in a clean, 12-qt. pail. One quart of this is spilled in the central work area of the floor. A freshly laundered mophead is used to scrub this area to solubilize dried blood or pus. The remainder of the detergent germicide is then spilled and spread to cover the periphery. After the entire floor is flooded, the film of water is removed with a wet pick-up vacuum cleaner. With minimal study, a pattern can be developed for flooding, spreading, and picking up that avoids walking in the wet area. In large operating room suites, a scrubbing machine that automatically dispenses the detergent germicide is time-saving and convenient. A wet pick-up vacuum cleaner is essential to remove the slurry of dirt and bacteria that is loosened from the floor. In this way, a grossly clean and bacteriologically safe floor is attained. The bacteriological count on the unused surface of the floor 12 hours after this cleaning process should be less than five organisms per square centimeter. There should be no dust. The operating room furniture, including the castors, is wiped with a cloth dampened in a germicide, prior to returning it to the clean room. The center of the operating room floor is cleansed with a mop moistened with detergent germicide immediately after each operation. This mop is kept in a flushing rim service sink located in the sterilizing room adjacent to the operating room. The mop must not be stored with used cleaning solution. The textile and dirt deplete the germicide, and bacterial multiplication occurs. This results in painting the floor with bacteria. Mops used in the operating room must be laundered daily.

CONTACT LENSES FOR YOUNG CHILDREN

To the Editor:—*Are contact lenses recommended for treatment of simple myopia in teenagers or younger children? Is this age a contraindication?*

M.D., South Carolina.

Answer.—Until recent years, this consultant has been inclined to advise against contact lenses for children. More recently, with some refinements in contact lenses and with the increased recognition that social acceptance in the early teens is most important to children in this age group, this attitude has become more lenient. Contact lenses for children in their early teens may be prescribed under certain conditions. The corneal contact lens gives a better cosmetic effect and is tolerated better, but it offers less protection to the eye than does the scleral contact lens. The corneal contact lens is not adaptable for sports or swimming, while the scleral contact lens, which is not as good cosmetically, may serve an excellent purpose. Recently, it has been suggested (but without reasonable proof or confirmation) that contact lenses may have some influence on the course of simple myopia. This has yet to be corroborated.

HERPETIC LESION AND MENSTRUATION

To the Editor:—*What is the cause and treatment of mouth ulcers which begin about the time of ovulation and stop just before menses? They have been present since puberty in a 33-year-old woman. Her health otherwise has been normal since correction of a hypothyroid state with thyroid extract, and this treatment improved the mouth situation a little. The ulcers begin as small blebs. On alternate months they are worse —more of them and seemingly more inflammation secondarily. During two pregnancies there have been no ulcers, but they have returned immediately after delivery.*

Haywood L. Moore, M.D., Brunswick, Ga.

Answer.—Although ulcers of the mouth occurring before menstrual periods have been described for many years as recurrent or habitual herpes of the mouth, the herpetic etiology has not been definitely proved and, in fact, is denied by Blank and associates (Letter to the Editor, *J. A. M. A.* 142:125 [Jan. 14] 1950) and by others. The distinction of herpetic lesions from etiologically different but similar types of recurrent stomatitis depends on the isolation of the virus and/or results of biopsy. Circulating antibodies to the herpetic virus are of importance more by their absence than by their presence and, indeed, are frequently absent in recurrent ulcers of the mouth. It has long been observed that the skin and mucous membranes are affected by the changing hormonal activities of the menstrual cycle. The mucosa of the oral cavity reflects these influences in a fashion similar to but not as demonstrable as that of the vaginal mucosa. Since the cause of recurrent ulcers is not known, aside from the definite but uncommon reaction to some foods, the one practical point of attack in this patient would seem to be on the menstrual cycle itself. The time relation here, after ovulation and when progesterone is greatest in amount, suggests that suppression of ovulation by estrogen therapy for a few cycles might be of benefit.

MENTAL RETARDATION

To the Editor:—*A 3-year-old girl does not yet speak, although otherwise she is apparently of normal intelligence. The parents are healthy, and pregnancy was normal. The patient, whose delivery record states, "cord around the neck of the baby," was born in asphyxia, and convulsions occurred during the first two days of life. When the patient was one day old, a lumbar puncture resulted in a normal-looking liquor (no gross hemorrhage). There was delay in her sitting up and walking, and now there is considerable delay in her starting to speak. She has now a vocabulary of 15-20 words (such as mommy and water), but she generally uses words which are not understood by the parents. Physical development, including hearing, is good, and the general intelligence is considered average. She started to use toilet facilities at the age of 2 years. Electroencephalographic study revealed beta waves generally of low amplitude and dysrythmia over the left hemisphere and no or minimal electric activity over the left parieto-occipital area. Some damage is demonstrable over the right occipital area as well. A neurologist who was consulted suggested small doses of x-ray therapy (4×100 r, to be repeated twice in two-month intervals). He claims to have seen good results in such cases. What is the prognosis of this condition? What therapy can be recommended? Is there any danger of further damage by a trial of x-ray therapy with the dosage indicated above?*

M.D., Washington, D. C.

Answer.—The cyanosis at birth and the early convulsions point to cerebral anoxia as responsible for the present mild mental retardation. The electroencephalogram as reported is of questionable significance. There would seem to be no rationale for (because of fewer side reactions), methylprednisolone, 4 mg., or triamcinolone, 4 mg. After several days the dose is gradually reduced and the smallest effective dose continued indefinitely with occasional rest periods to determine whether it is still needed. Other measures should not be neglected: prohibition of tobacco, bronchodilators, such as aerosols of adrenalin or isoproterenol, antibiotics for infection, digitalization for cor pulmonale, and, especially, perfection of diaphragmatic breathing. The patient taking corticosteroids should be observed for hypercortisonism, although this does not occur frequently with small doses and with the newer compounds.

TONSILLECTOMY AND STEROID MEDICATION

To the Editor:—*Is tonsillectomy contraindicated in a child who is taking steroid therapy for acute rheumatic fever if the sedimentation rate has returned to normal and if the child is operable in all other respects?*

J. J. Johnson Jr., M.D., Las Vegas, N. Mex.

Answer.—There is no contraindication to tonsillectomy in a child who has been receiving steroid therapy, within the circumstances stated. However, if the patient is still receiving steroid therapy, the preoperative preparation should be considered very carefully by an internist or pediatrician experienced in such problems. If the therapy has been stopped for three months or longer, a physician experienced in steroid therapy should evaluate the case as to whether preoperative preparation is necessary; if preoperative preparation is not given, he should be available for emergency treatment during and after the operation. This requirement should hold for a year after discontinuation of steroid therapy.

THE PINEAL BODY

To the Editor:—*Please give information regarding recent opinions on the pineal body. What is its function? Does it secrete a hormone? Is it a vestigial third eye?* *M.D., Canada.*

Answer.—Authorities are now generally agreed that the pineal body does not secrete a hormone. Tumors of the pineal body have often been found in association with sexual precocity, especially in males. It is thought, however, that these effects come about through pressure on the hypothalamic center and contiguous areas. There is no reference in any of the recent textbooks to a vestigial third eye.

APPEARANCE OF PHYSICIANS IN PUBLIC

To the Editor:—*The answer to the question concerning public appearance of physicians in* The Journal, *March 29, 1958, page 1666, is timely and enlightening. But please comment further on a specific aspect of the same question. Suppose a state university establishes, controls, and operates a noncommercial, educational television station and asks the faculties of its component colleges to produce popular programs in various fields of their competence. Would it be ethical for the university's college of medicine to participate in such an undertaking? Participation would involve members of the faculty appointed by the dean in a 30-minute weekly discussion on such subjects as health and disease, medical progress, and medical education. Medical subjects would be presented by full-time employees who do not maintain private offices and who accept as private patients only those persons referred by other physicians.* *M.D., Illinois.*

Answer.—The answer to this specific question is also contained in the answer to the original question. Even if the physicians participating did have a private practice, it would still be ethical for them to participate. The "Principles of Medical Ethics," published June, 1955, defines the duties of physicians to the public media of information in section 5 of chapter 1 in the following words: "The medical profession considers it ethical for a physician to meet the request of a component or constituent medical society to write, act, or speak for general readers or audiences. On the other hand, it may often happen that the representatives of popular news media are the first to perceive the adaptability of medical material for presentation to the public. In such a situation the physician may be asked to release to the public some information, exhibit, drawing, or photograph. Refusal to release this material may be considered a refusal to perform a public service, yet compliance may bring the charge of self-seeking or solicitation." With relation to the specific question now asked, the following paragraph from the same chapter is definitive: "An institution may use means, approved by the medical profession in its own locality, to inform the public of its address and the special class, if any, of patients accommodated." These "Principles of Medical Ethics" have been superseded by the shortened code, in which section 10 reads as follows: "The honored ideals of the medical profession imply that the responsibilities of the physician extend not only to the individual but also to society, where these responsibilities deserve his interest and participation in activities which have the purpose of improving both the health and the well-being of the individual and the community." The only criticism this consultant has of the situation presented in the question is on grounds of showmanship rather than ethics. The kind of program envisioned would be fully as dull as it would be ethical.

WASHINGTON NEWS

FROM THE WASHINGTON OFFICE OF THE AMERICAN MEDICAL ASSOCIATION

Defense, Military Officials Oppose Medicare Restrictions . .

AMA Witnesses to Testify on June 27 on Forand Legislation . .

Senate Leaders Oppose Making Single Agency of FCDA & ODM . .

SECRETARY McELROY OPPOSES MEDICARE RESTRICTIONS

The controversy over the future of the uniformed forces dependents medical care program has taken a new turn. At the very outset of hearings before a Senate appropriations subcommittee, Defense Secretary McElroy, followed by Army Secretary Brucker, let it be known that the administration favors eliminating restrictive language written in the House version.

Mr. Brucker testified that setting a 60 million dollar limitation—in the face of an estimated 90 million dollar cost for the program—on civilian medical and hospital care could cause "the eventual destruction of the medicare program." In addition the House proposes greater utilization of military facilities by dependents.

The Army Secretary testified that while he was in agreement with greater use of military facilities, "we had hoped this could be achieved by competitive means, and we believe that this method would, in time, bring about a desirable distribution of dependent patients between uniformed services and civilian medical facilities."

But he went on to stress that any specific dollar limitation would completely change the concept of the program, and implementation conceivably could not be effected in time to insure that such limitation would not be exceeded. Mr. Brucker emphasized that the cost of dependents care is not known to the government until the doctors' and hospitals' claims are presented. "It would be most difficult to insure that a limitation would not be exceeded unless civilian medical care is controlled by preauthorization for each individual patient or unless the scope of care authorized is reduced to such a level that there would be no possibility of the cost exceeding the limitation," the Secretary told the subcommittee headed by Senator Chavez (D., N. Mex.)

The subcommittee then was informed that the Secretary of Defense was prepared to take the following three steps to insure more use of military facilities:

1. Direct the Secretaries of Army, Navy, and Air Force to instruct commanders of posts, camps, and stations to require dependents living on reservations or in Wherry or in Capehart housing to use uniformed forces medical services, "subject to the availability of space, facilities, and the capabilities of the medical staff."
2. Reduce the medical care coverage in civilian facilities by eliminating certain types of care now authorized. It is understood the department has in mind tightening up on elective surgery.
3. Consider increasing the monetary liability beyond the present $25 deductible for civilian medical care, "thus influencing more of them to choose uniformed services medical facilities."

On this last point, Defense may ask Congress for an amendment to the medicare act, "at such time as the Secretary of Defense determines that the monetary liability of the dependents should be increased."

The American Medical Association and the American Hospital Association have joined in making a strong plea to Congress to preserve the program as Congress authorized it two years ago. Otherwise, a basic principle, that of free choice of physician, will be violated, the associations point out.

The restrictive section under attack by both the profession and the armed forces states that the Defense Department could spend no more than 60 million dollars for medicare in civilian hospitals and using civilian doctors. The budget request for this part of the program has been $71,900,000, although revised estimates place the cost at 90 million dollars for the next fiscal year.

A. M. A. WITNESSES TESTIFY JUNE 27 ON FORAND BILL

After a week of testimony on other social security subjects, the House Ways and Means Committee next week will consider bills designed to increase dollar or service benefits, including the Forand bill for free hospitalization and surgical services for social security beneficiaries.

Most witnesses the fist week were concerned with changes in the public assistance program and permanent amendments for the federal-state unemployment compensation system.

Spokesmen for the American Medical Association on June 27 will be Trustee Leonard Larson and Dr. Frank Krusen of the Mayo Clinic, a leader in rehabilitation. Also to be heard that day will be representatives of the American Hospital Association, American Dental Association, American Nursing Home Association, American Nurses Association, Inc., and Physicians Forum.

The A. M. A. and other associations in the health fields oppose the Forand bill because it proposes to solve the problem of the medical care of the aged through an expensive and politically dangerous experiment. It is their contention that a lowering of the age for medical benefits would bring about total national health insurance. They believe the problem can be solved through extension of voluntary health insurance and other methods, many of which now are under study by the Joint Commission to Improve the Health Care of the Aged.

Representatives of the AFL-CIO and the National Association of Manufacturers also will testify next week.

OPPOSITION ARISES TO MERGER OF FCDA AND ODM

The administration's plan for combining the Federal Civil Defense Administration and the Office of Defense Mobilization into a single agency has come up against some opposition from leading Senators. Chairman Hubert Humphrey (D., Minn.) of the Senate government operations subcommittee fears civil defense would lose its identity. Sen. Charles E. Potter (R., Mich.) has reservations over placing a new operating agency directly under the President because of the many responsibilities he now has.

Senator Potter is the author of a resolution disapproving the projected merger into the Office of Defense and Civilian Mobilization. The plan goes into effect July 1 unless either House or Senate votes the resolution of disapproval. The opposition arose at a hearing of Senator Humphrey's subcommittee.

The plan was stoutly defended by administration officials, including Gordon Gray, head of the Office of Defense Mobilization, and Leo A. Hoegh, FCDA administrator. William F. Finan, a witness from the Budget Bureau, argued that it would eliminate "present confusion in our nonmilitary defense program" and result in "far greater effectiveness in dealing with what we now recognize to be the inseparable jobs of planning for civil defense and defense mobilization preparedness."

DULLES APPEALS FOR MEDICAL PROGRAM FOR FOREIGN SERVICE AND DEPENDENTS

Testifying before the Senate Appropriations Committee on the Senate Department's budget, Secretary Dulles appealed for establishment of a medical benefits program for dependents of foreign service personnel.

In justification, the Secretary described the "primative conditions" under which Foreign Service officers and their families have to live.

He declared:

"In comparison with our own history, the conditions would take one back to the middle of the last century, in terms of health hazards, sanitation, and the availability of schools and hospitals and other community services and amenities which most of us take for granted.

"The absence of such a simple thing as a reliable source of pure and potable water is a serious problem in many countries of the world. The incidence of disease, particularly diseases affecting children, is high in many areas in which we require our personnel to serve. These are some of the reasons why I believe it necessary to urge upon the Congress greater assistance to the staff of the Foreign Service in the form of recreational facilities, medical benefits for dependents, and other special allowances in hardship and unhealthy posts."

LEGISLATION TO AID HOSPITALS AND NURSING HOMES ADVANCES

Subcommittees of the Senate and House have acted to help hospitals, nursing homes, and chronic disease facilities in their financing problems.

A subcommittee of the Senate Banking and Currency Committee, headed by Sen. John J. Sparkman (D., Ala.), has recommended to the full committee that the federal government guarantee loans for proprietary nursing homes and other facilities for the aged, and also has approved increasing from 25 to 100 million dollars a fund earmarked for low interest loans to hospitals for building housing for student nurses and interns.

Approval of loan guarantees for nursing homes is in line with recommendations of the American Medical Association in testimony presented earlier by Dr. R. B. Robins, a former vice-president of the Association.

Proprietary nursing homes, which handle a high majority of all nursing home cases, have complained that they are unable to obtain private financing on reasonable terms, because they are "single-purpose" structures and therefore not attractive as a straight commercial credit risk.

The subcommittee proposed that the U. S. guarantee mortgages up to 75% of the value of the structures, the ratio requested by the American Association of Nursing Homes. The bill would apply the association's definition of nursing homes.

In a separate action, the health subcommittee of the House Interstate and Foreign Commerce Committee approved low interest loans for nonprofit hospitals, to be tied in with the Hill-Burton grant program. The legislation was introduced at the request of some religious groups that want assistance in building, but are morally opposed to accepting gifts from a government. Applicants for loans would have to meet the same requirements as other Hill-Burton applicants.

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ELECTROENCEPHALOGRAPHIC STUDY OF PERSONS BEFORE AND AFTER POLIOMYELITIS VACCINATION

Erna L. Gibbs
and
Frederic A. Gibbs, M.D., Chicago

Electroencephalograms were obtained from 852 normal subjects before and after the first, second, and third inoculations with Salk vaccine for poliomyelitis. The series included infants, children, adolescents, and adults. No electroencephalographic abnormalities were induced by the vaccination in initially normal people. The possibility that vaccination might cause detectable injury in brains already handicapped by previous disease or injury was also investigated. A group of 106 persons with brain disorders, including 44 with epilepsy, were studied electroencephalographically. Again no evidence of harm from the vaccination was obtained. The vaccines used in this study were commercial preparations from two drug companies, and the evidence showed that these preparations could be given safely to patients with or without manifestations of preexisting cerebral disease.

In 1956, shortly after a program of mass vaccination for poliomyelitis with Salk vaccine was started in the Chicago area, reports began to circulate of children who had developed convulsions or other signs of central nervous system disorder supposedly as a consequence of vaccination. One of the first cases to come to our attention was that of a 14-year-old boy who became seriously ill two days after receiving his second injection of Salk vaccine. His condition deteriorated rapidly and ended in death. The report of this spread rapidly through the community. The full clinical history, however, revealed that the patient had had enuresis since birth. He had had chronic pyelonephritis with severe hypertension and extensive encephalopathy. He developed a severe pain in the left flank the day before the second Salk vaccination. The postmortem diagnosis was pyelonephritis with overwhelming sepsis and uremia. It seemed unlikely, in this case, that the Salk vaccination was causally related to the final illness.

To track down every patient who develops convulsions or other symptoms as an apparent untoward reaction to Salk vaccine in order to determine whether or not the vaccination was actually the cause would be difficult or impossible. Seizures of various types are so common in children that cases are certain to be encountered where the time relationship between the first epileptic seizure and the Salk vaccination would make the vaccination a "reasonable presumptive cause." Sudden inexplicable illnesses, some of which defy even the most expert diagnosticians, occur in a large number of children. By coincidence, an unexplained illness could follow a Salk vaccination at just the right time to convince the family and even the physician in charge that the vaccination was responsible for the child's illness or even his death.

TABLE 1.—*Electroencephalographic Study of 852 Persons Receiving Salk Vaccine*

	Recordings Before and After Injection, No.			
Age, Yr.	1st	2nd	3rd	EEG Change
<1	32	32	20	-
1-2	52	62	70	-
3-5	110	110	182	1
6-10	53	53	183	-
11-15	120	120	197	-
16-19	81	81	81	-
20+	121	121	119	-
Total......	569	569	852	

Does Salk vaccine, when administered as part of a program of mass immunization against poliomyelitis, cause brain disorder in some persons? This question seemed worth answering. The electroencephalogram is a sensitive indicator of acute encephalitic types of reaction. A great variety of viruses produce abnormal slow activity in the electroencephalogram during the acute and immediate postacute stages of virus infections, even when no clinical evidence of encephalitis is present.[1] Vaccines of various types, for example, rabies and also the triple vaccine of whooping cough, diphtheria, and tetanus, can produce brain disorder and, with it, definite electroencephalographic abnormalities.[2] It seemed desirable to proceed with a controlled encephalographic study of patients receiving Salk vaccine.

Material and Method

Arrangements were made to obtain electroencephalograms of infants, children, adolescents, and adults before and after the first, second, and third inoculations with Salk vaccine. Commercial preparations from two drug companies were used. In each vaccination, 1 cc. of Salk vaccine was given intramuscularly. To guard against the possibility of preexisting electroencephalographic abnormality going unrecognized, to be picked up after vaccination, we carried out careful preliminary electroencephalographic study on all patients. Recordings were made with patients in the waking and the sleeping states with leads in the frontal, parietal, temporal, and occipital areas on both sides. Recordings were made 24 hours after the vaccination in three-fourths of the patients and 48 hours after the vaccination in one-fourth. In a few cases recordings were made at daily intervals for four days after vaccination.

The number of normal subjects obtained in each age group and the number of recordings before and after the first, second, and third inoculations are indicated in table 1. A group of patients with epilepsy and/or brain damage was also studied, because it seemed possible that such persons might be more sensitive to Salk vaccine than persons with normal brains; the age distribution of this group is shown in table 2.

Some difficulty was encountered in finding 2-to-5-year-old children in the Chicago area who had not received first and second vaccinations. This is a tribute to the thoroughness of the mass vaccination program in the years 1956 and 1957. We discovered that children who had not already been vaccinated usually came from families with a general prejudice against scientific medicine and a particular prejudice against medical research. Although electroencephalographic studies are not painful, the need for them in the present instance was hard to explain without arousing suspicion or alarm. The troublesomeness of six visits for the before-and-after electroencephalograms, as compared with only three visits for the usual Salk vaccination, was a powerful deterrent to parents and subjects.

Stations for electroencephalographic studies were set up in the following hospitals: Chicago Municipal Contagious Hospital, Cook County Hospital, Illinois Neuropsychiatric Institute, and Rockford Memorial Hospital. The Morton High School and the Nazareth Academy installed temporary electroencephalographic laboratories for this study. A station was also set up in the office of Dr. John Kendrick in Richmond, Va. The recordings from the Rockford and Richmond areas were used to check on the possibility that local conditions, for example, the recent poliomyelitis epidemic in Chicago (1956), might affect the results.

Results

In only one case, considered in detail in a later paragraph, was the electroencephalogram significantly altered. This is astonishing. We had not expected to obtain such completely negative results with a biologically potent material. One child wit cerebral palsy died of pneumonia (unrelated to va cination) after the second inoculation. Two childre with brain disorder moved out of Chicago befo the third inoculation.

TABLE 2.—*Electroencephalographic Study of 106 Persons with Brain Disorder Receiving Salk Vaccine in Whom No Electroencephalographic Change Was Observed**

	Recordings Before and After Injections		
Age, Yr.	1st	2nd	3rd
<1	9	9	9
0-2	30	30	29
3-5	25	25	23
6-10	20	20	20
11-15	13	13	13
16-10	1	1	1
20+	8	8	8
Total..............	106	106	103

* 44 with epilepsy; 24 with cerebral palsy; 38 with other disorders.

In two cases we received alarming reports th the child had developed clinical symptoms whic prevented his return for the postvaccination r cording. On checking up on these two cases, however, we found that in one case the child was entirely well and his mother had only wished to avoid the trouble of bringing him in for further study. In the other case, the mother mistook the symptoms of an uncomplicated upper respiratory infection for a postvaccination reaction.

One child, 5 years of age, developed slow waves in his electroencephalogram 24 hours after his third shot. It was feared that this might be a reaction to the vaccine. He had a fever at the time of the recording, and in the next five days he went through the typical course of an attack of Asiatic influenza. His symptoms were identical with those of the other members of his family who also contracted this disease. We saw numerous patients with an encephalitic type of reaction to Asiatic influenza. Usually in these cases the slow activity is transitory; this child's electroencephalogram normalized within a few days. However, the experience made us decide not to complicate our study by continuing Salk vaccinations during the epidemic of Asiatic influenza.

Summary and Conclusions

Electroencephalographic study of 852 normal infants, children, adolescents, and adults indicates that Salk poliomyelitis vaccine produces no electroencephalographic abnormalities. This gives assurance that Salk vaccine is unlikely to cause an encephalitic type of reaction or brain injury. Electroencephalographic study of 106 patients with epilepsy and with brain damage indicates that such patients can be safely given Salk vaccine.

912 S. Wood St. (12) (Dr. F. A. Gibbs).

This study was aided, in part, by a grant from the National Foundation for Infantile Paralysis.

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INTRACRANIAL ANEURYSM IN THE GERIATRIC PATIENT

REPORT OF THREE SURGICALLY TREATED PATIENTS

Edmund A. Smolik, M.D.
and
Francis P. Nash, M.D., St. Louis

One of the most common stigmata of aging is the occurrence of vascular degenerative changes which are often most pronounced in the intracranial blood vessels. Incident to these vascular degenerative changes, secondary pathological changes may develop, such as arteriosclerotic intracranial aneurysm.[1] Since there is a progressive increase in the number of patients entering the geriatric span of life,[2] it would seem logical to expect a corresponding increase in the number of patients with such intracranial aneurysms. A perusal of the available literature does not reveal a wide surgical experience in the management of this particular type of aneurysm (arteriosclerotic) in this particular age group. We therefore thought it of interest to report our surgical experience in the management of three cases of proved intracranial aneurysm developing in patients in the seventh and eighth decades of life.

Intracranial aneurysms were demonstrated in three patients, aged 66, 76, and 77. Because of the unendurable pain and advancing neurological deficits surgical intervention became mandatory. The authors present the details of their surgical management of these cases. The article serves to emphasize the occurrence of intracranial aneurysms in the geriatric patient and the possibility that such vascular lesions may become more frequent in an aging population.

Report of Cases

Case 1.—A 66-year-old woman was examined because of the complaints of headache, nausea, and vomiting. The medical history was negative with the exception of "pneumonia" two years previously. The patient was alert and oriented. The blood pressure was 146/68 mm. Hg; pulse rate, 84 per

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From the Department of Surgery (Section of Neurosurgery), St. Louis University School of Medicine.

minute; and respiratory rate, 24 per minute. There was ptosis of the right eyelid (fig. 1), and hyperesthesia to pinprick over the supraorbital and maxillary areas on the right. The neurological examination was otherwise normal. X-rays of the skull and chest were normal. Urinalysis showed a trace of albumin but was otherwise negative. The hemoglobin level was 9.9 Gm. per 100 cc. The hematocrit was 32%. The blood urea nitrogen level was 20 mg. per 100 cc. The fasting blood sugar level was 131 mg. per 100 cc. The serologic tests were negative.

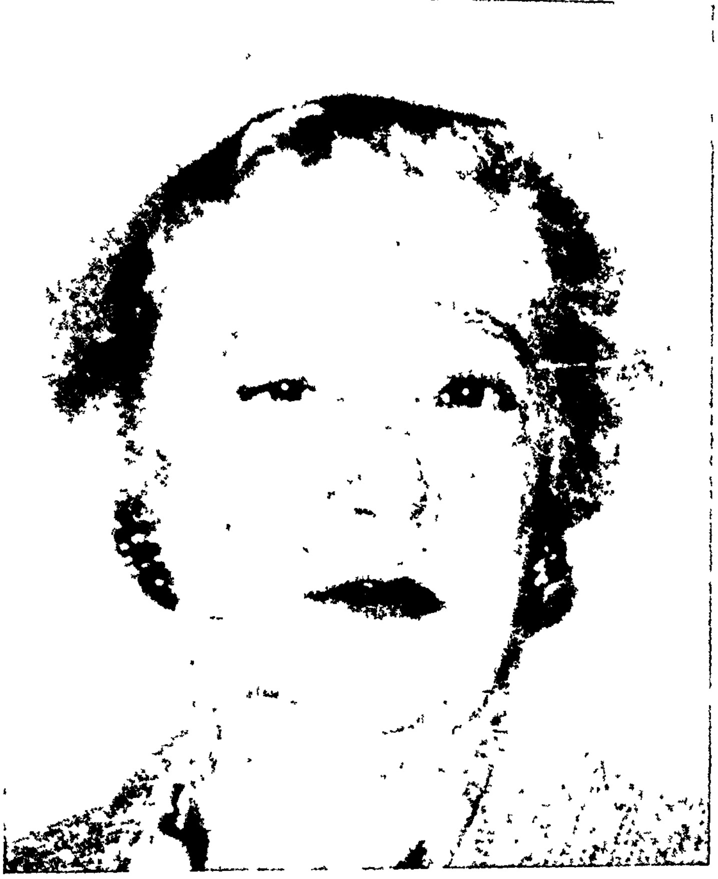

Fig. 1 (case 1).—Ptosis of right eyelid.

A diagnosis of intracranial aneurysm was made. A right cerebral arteriogram was done under thiopental (Pentothal) anesthesia, percutaneously, using 50% diatrizoate (Hypaque) as the contrast medium. A large aneurysm of the right internal carotid artery was demonstrated (fig. 2). Four days after angiography, the patient was taken to surgery where the right common carotid artery was exposed. A Poppen-Blalock arterial clamp was placed about the vessel. After preliminary stellate ganglion procaine (Novocain) block and periarterial procaine irrigation, the clamp was tightened to produce about 50% occlusion of the arterial lumen. The patient tolerated the procedure without difficulty. The patient was returned to the ward and placed in a cooled oxygen tent. In addition, she was given regular intramuscular doses of papaverine and large doses of vitamin B complex.

Twenty-four hours later the clamp was tightened to reduce further the remaining volume of carotid blood flow. The patient tolerated this without incident. Seventy-two hours after placement, the clamp was closed to produce total arterial occlusion. No neurological deficits developed. Three days later the patient was returned to surgery where double chromic ligatures were placed about the common carotid artery both above and below the point of clamp occlusion. The arterial clamp was then removed. The patient was discharged from the hospital 10 days later free of pain but with ptosis of the right eyelid. The patient has remained pain free. Since her discharge there has been complete recovery from ptosis of the eyelid (fig. 3).

Case 2.—A 77-year-old woman was admitted to the neurosurgical service because of persistent left-sided headache of insidious onset about six months prior to admission. Since that time the pain had persisted and had not responded to symptomatic therapy. The patient was currently receiving treatment for hypertension and cardiac decompensation. The medical history was negative except for bilateral simple mammectomy in 1910 for "cystic disease of the breasts."

The patient was alert and oriented. The blood pressure was 190/110 mm. Hg; pulse rate, 100 per minute, respiratory rate, 20 per minute. There was an incomplete ptosis of the left eyelid; the neurological examination was otherwise normal. X-rays of the skull were normal. The chest plate showed a moderate cardiac enlargement with minimal aortic calcification. The hemogram was normal. The urinalysis was normal except for a "slight trace" of albumin. The blood urea nitrogen level was 20 mg. per 100 cc. The fasting blood sugar level was 118 mg. per 100 cc. The serologic test was negative. An electrocardiogram was interpreted as showing left axis deviation with evidence of myocardial change.

A diagnosis of intracranial aneurysm was made. Clinically the patient was a poor risk for any surgical procedure. However, her head pain was of such an unbearable nature that she requested some effort be made to give her relief, although the dangers of any such procedures were understood. Accordingly, a left carotid cerebral arteriogram was done, percutaneously, under thiopental anesthesia, using 50% diatrizoate as the contrast medium. A large intracranial aneurysm was outlined arising from the left internal carotid artery. Four days after arteriography, the patient was taken to surgery where the left common carotid artery was exposed. After procaine block of the stellate ganglion and periarterial procaine irrigation, a Poppen-Blalock clamp was placed about the artery and closed to produce about 50% arterial occlusion. The patient tolerated the procedure without difficulty. She was returned to the ward where treatment included high concentration of cooled oxygen per tent. In addition, she was given papaverine parenterally and large doses of vitamin B supplement.

Fig. 2 (case 1).—Right cerebral arteriogram demonstrating aneurysm of right internal carotid artery.

Twenty-four hours later the Poppen-Blalock clamp was tightened to occlude about one-half of the remaining arterial lumen. No neurological deficits developed. The following day the arterial clamp was completely closed. Two hours after this the patient "fainted" and developed hemiparesis on the right side. These were transient changes and the patient reportedly rapidly recovered consciousness with no obvious motor weakness. No report was made of this incident by those in immediate attendance. Eight hours later the patient abruptly developed a total aphasia and hemiplegia on the right side. The arterial clamp was immediately fully opened. In spite of this, the hemiparesis and aphasia persisted and the conscious level deteriorated. The stupor persisted. The patient died 30 days after total arterial occlusion. No autopsy was permitted.

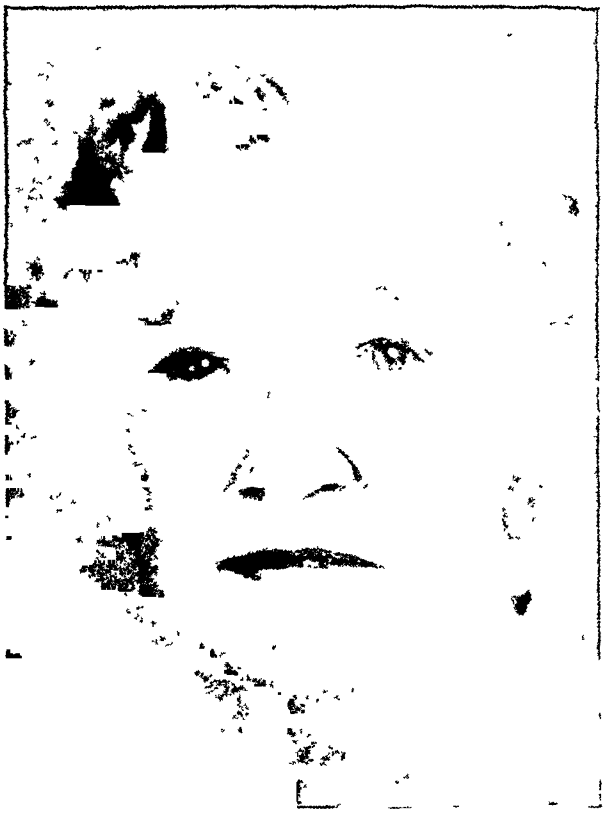

Fig. 3 (case 1).—Recovery from ptosis of right eyelid postoperatively.

Case 3.—A 76-year-old male was admitted to the neurosurgical service because of "sticking pains" behind the left eye and a "droop" of the left eyelid. The patient first experienced a sudden, severe, left retro-orbital pain about two months prior to admission. Thereafter he noticed his "left eye began to droop." Three days after onset of pain, the ptosis was complete. The pain persisted. The patient was a known diabetic of 15 years' duration. He required no insulin therapy but was controlled by dietary measures. Five years prior to this examination he had a transurethral resection for benign prostatic hypertrophy.

The patient was alert and well oriented. The blood pressure was 150/70 mm. Hg; pulse rate, 72 per minute. There was a complete ptosis of the left eyelid (fig. 4). The left pupil was dilated and there was lateral deviation of the left eye. There was loss of upward, downward, and inward ocular movements on the left. The neurological examination was otherwise normal. The x-rays of the skull and chest were normal. The hemogram was normal. The urinalysis showed no abnormalities. The blood urea nitrogen level was 23 mg. per 100 cc. The fasting blood sugar level was 83 mg. per 100 cc. The serologic test was negative. A diagnosis of intracranial aneurysm was made. A left carotid cerebral arteriogram was done, percutaneously, with the patient under thiopental anesthesia, with use of 50% diatrizoate solution as the contrast medium. A large aneurysm arising from the left internal carotid artery was demonstrated (fig. 5).

Three days after arteriography, the patient was taken to surgery where the left common carotid artery was exposed. After procaine block of the left stellate ganglion and procaine irrigation of the periarterial tissue, a Poppen-Blalock clamp was placed about the artery, then tightened to produce about 50% occlusion of the arterial lumen. The patient tolerated the procedure without difficulty. Postoperatively, his treatment included the use of high concentrations of cooled oxygen per tent. In addition, the patient was given papaverine intramuscularly and large doses of vitamin B supplement. Twenty-four hours later the clamp was tightened to further reduce carotid blood flow.

The next day the clamp was completely closed. No neurological deficits developed. Twenty-four hours later the patient was returned to surgery, where double chromic sutures were placed about the common carotid artery both proximal and distal to the point of clamp occlusion. The patient tolerated the procedure without incident. He was discharged from the hospital free of pain five days after ligation. The oculomotor paresis persisted. Since discharge, the patient has remained free of pain. There has been excellent return of oculomotor nerve function (fig. 6).

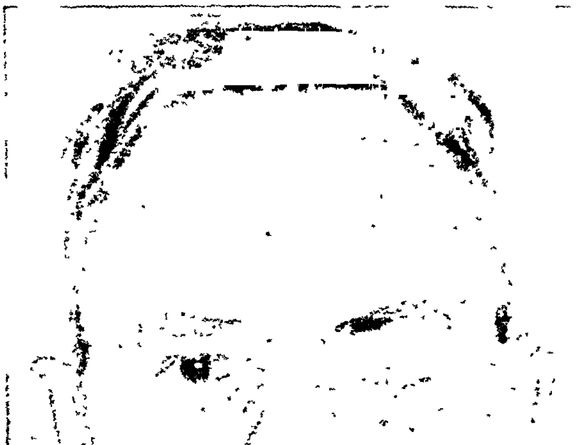

Fig. 4 (case 3).—Complete ptosis of left eyelid.

Comment

Three patients with intracranial aneurysm were respectively 66, 77, and 78 years of age. McDonald and Korb,[3] in culling the world's literature, found only 41 authenticated cases of intracranial aneurysm in people over 70 years of age. Later Dandy in his series[4] reported only seven patients beyond the age of 70 years. Other series[5] have listed a total of 200 cases of proved intracranial aneurysm with but one patient beyond the 70th year of age. In these reports only 14 patients were listed in the 0-through-70-year age group.

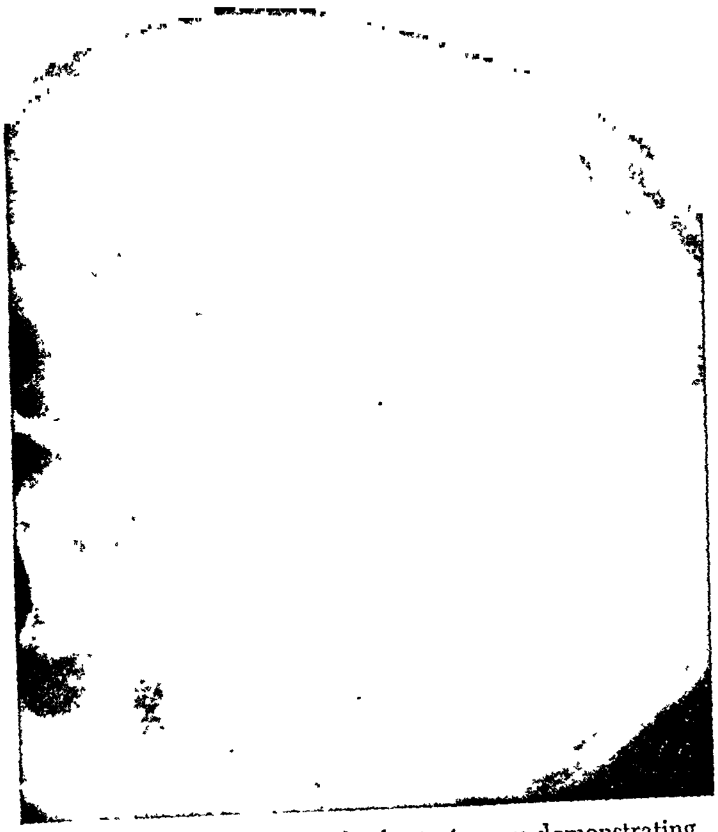
Fig. 5 (case 3). Left cerebral arteriogram demonstrating aneurysm of left internal carotid artery.

Other studies have shown that atherosclerotic vascular lesions are not uncommon at the site of origin of arteriosclerotic aneurysms.[2] As the individual lives to an older age with accompanying vascular changes, aneurysms of this origin may become more frequent. If the catastrophe of subarachnoid hemorrhage resulting from rupture of such aneurysms is to be avoided, the existence of the lesions must be suspected. The cases reported here may serve to focus attention on the occurrence of intracranial aneurysms in elderly patients.

In cases of suspected intracranial aneurysm, cerebral angiography is required to establish the diagnosis. The employment of the percutaneous carotid puncture, under thiopental anesthesia, and the use of 50% diatrizoate solution as the contrast medium[6] has reduced the trauma of this procedure to a minimum. Using these techniques, we do not consider advanced age, per se, as a contraindication to cerebral angiography.

The management of the elderly patient with a proved intracranial aneurysm presents a particular surgical challenge. The question of ligation of the carotid artery in the aged individual has been a focal point of controversy. On the one hand there have been those such as Dandy[7] and Cushing[8] who believed that in persons over 45 years of age, ligation of the internal carotid artery becomes increasingly hazardous. On the other hand, the reports of Pilcher and Thuss[9] among others described no increase in the incidence of complications after carotid ligation in elderly patients.

Our experience indicates that carotid ligation may be successfully employed in the treatment of aged patients with intracranial aneurysm. In our cases 1 and 3, the patient was completely free of pain and regained oculomotor nerve function after treatment by common carotid artery ligation on the involved side. In each case the Poppen-Blalock clamp was used for controlled carotid occlusion. During the course of carotid occlusion, supplemental therapy included the use of high concentrations of cooled oxygen, liberal amounts of vitamin B, glucose parenterally and papaverine intramuscularly. Where indicated, whole blood transfusions were judiciously used to increase the oxygen-carrying ca-

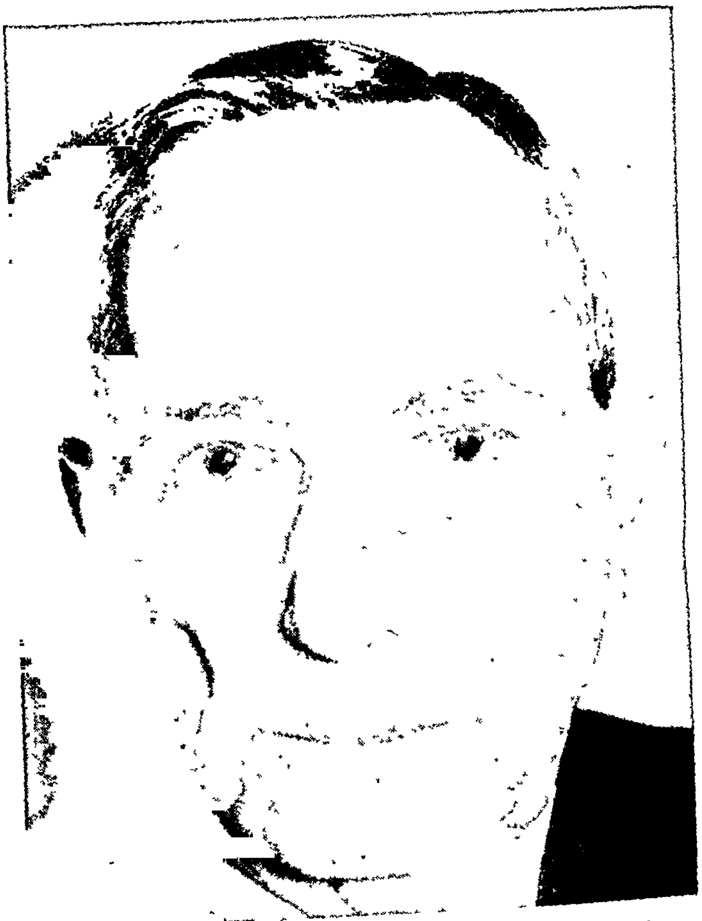
Fig. 6 (case 3).—Recovery of oculomotor nerve function postoperatively.

pacity of the blood. We believe that these adjuncts are important in the successful clinical management of such patients.

Recently Bassett and co-workers[10] have questioned the advisability of any form of surgical treatment in the elderly patient with intracranial aneurysm. These authors stated that "Not all angiographically verified aneurysms are amenable to surgical treatment; those encountered in elderly patients with advanced arteriosclerosis and hypertension are better left alone." We believe that in geriatric patients with advancing neurological deficits, or in instances where pain arising from these lesions makes life unbearable (case 2), surgical intervention may become mandatory.

Recently, Gurdjian and Webster[11] reported studies emphasizing the value of preligation carotid compression tolerance tests. These procedures may prove of value in averting some of the circulatory sequelae that may follow carotid ligation. Our single failure may have been averted if the significance of the "fainting spell" had been appreciated by those in immediate attendance, so that full carotid flow could have been immediately reestablished.

On the basis of our experience of an admittedly small group of patients, it appears that staged occlusion of the common carotid artery is useful in the surgical management of intracranial aneurysm in the aged patient. Although the advantages of direct surgical attack are understood, the narrowed physiological reserves of the elderly patient may preclude the use of this surgical approach.

The question of the most desirable anatomic level for arterial ligation in the neck has been studied.[12] The comparative value of internal carotid ligation versus common carotid artery ligation in the management of intracranial aneurysm is still moot. However, in a recent report, Davis and associates[13] concluded that there was little difference therapeutically between internal carotid and common carotid ligation in the surgical treatment of intracranial aneurysm.

The effect of rate of arterial occlusion on the carotid system hemodynamics has been studied.[14] There is conflict of opinion regarding the physiological advantages of graded arterial occlusion. Based on our experience, however, we feel that the use of the clamp technique allows for controlled occlusion of the involved artery and a means for immediate reestablishment of carotid flow if clinically required. Further investigation of this problem of surgical management of cerebral aneurysm in the aged patient is indicated.

Summary

In three cases of intracranial aneurysms occurring in the geriatric age patient, the surgical treatment consisted of staged occlusion of the common carotid artery, with successful experience in two of the three cases. Such lesions will in all probability be encountered more frequently.

100 N. Euclid (8) (Dr. Smolik).

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CHALLENGE OF FETAL LOSS, PREMATURITY, AND INFANT MORTALITY—ASSESSING THE LOCAL SITUATION

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A concerted study by various agencies in New York City in 1933 started a campaign to reduce maternal mortality. The goal initially set was ultimately surpassed; by 1945 the mortality had fallen below the previously assumed minimum of 17 per 10,000 live births. Nevertheless the cause of maternal death is still in many instances recognized as a preventable one. Infant mortality likewise has been greatly reduced by comparison with the appalling figures for 1915, but recent progress in reducing neonatal deaths, particularly deaths in the first week of life, has been slight. The highest mortality rates in New York, for mothers and infants alike, are from districts with poor socioeconomic status. Within given categories of hospitals influenced by population composition a range of perinatal mortality is exhibited. The program for improving the care of premature infants has saved many lives, but postneonatal morbidity is still serious and the postneonatal mortality for prematurely born infants has not declined appreciably. The mechanisms that precipitate early labor are not entirely understood, and common sense demands an enlarged, coordinated research attack on these fundamental problems. Serious problems also exist in hospitals, especially due to the shortage of staff members. Prenatal clinics must be improved. Better teamwork among physicians and ancillary workers is needed in the maternity services, and more extensive facilities and additional nurses are needed for the care of the prematurely born infant. Continuing special attention must be given to the emergency problems created by the immigration of so many underprivileged people into the city. The ideal should be to give economically underprivileged babies the same chance for life and health that other babies have.

For too long a time, late fetal and early neonatal deaths have been considered separately. However, the deaths that occur just before, during, and just after the process of birth are all associated with the same biological process. It obviously makes great sense to look at them as an entity. The newer concept of "perinatal mortality" is therefore a useful and important one.

The term "perinatal mortality" is used somewhat differently by different persons, but this fact is not of great importance. The word "peri" means "around." In using it, some go back a little further from the moment of birth, others go forward a little further. The important fact is that all the deaths associated with the child-bearing process are here viewed simultaneously.

New York City figures are of interest, for they have a certain degree of accuracy not always obtainable in studies involving a total population in a community. For many years the Health Department has worked closely with the medical societies, hospitals, and physicians in the city. Together they have worked out a system of reporting a great deal of information concerning the medical condition of the mother and child at the time of birth and death a confidential medical report which is attached birth and death certificates. These reports are d only for statistical and scientific purposes. Re-ing is unusually complete, and, although the terial on the certificates is certainly not as accurate as that obtained by firsthand review of clinical records or contemporary scientific study, yet many of the errors are unquestionably compensated for by the large numbers involved.

The observations to follow are based on analyses made of the materials reported by physicians in these confidential medical reports of all births in New York City. The methods used for obtaining mortality rates are shown at the foot of each table. Such data, based on a total population in a community of 8 million persons, lend themselves to certain analyses not possible with data from smaller or more selected groups, such as patients in hospitals or members of group insurance plans.

In 1955, in New York City, 165,150 babies were born. Of these, 4,268 died before reaching their first birthday, and of these deaths more than two-thirds (2,921) occurred in the first week of life. Coupled with the loss of liveborn infants was the loss of viable fetuses of 28 weeks' gestation and over.

From the New York City Department of Health.
Read in part before the Annual Meeting of the Association for the Aid of Crippled Children, New York, April 30, 1956.

These fetal deaths amounted to 2,233 in 1955. These two groups of deaths (totaling 5,154) will be considered together as an entity with the descriptive designation of "perinatal" mortality. Numerically the perinatal deaths (5,154) constitute a larger group than fatalities due to accidents (3,034), tuberculosis (1,084), or diabetes (1,698). The reduction of perinatal mortality quite properly is, therefore, a challenge, and the time has certainly come for a consolidated attack on the problem of reducing the loss of life in this period.

Maternal Mortality

Since the health of the mother is important to the survival of the infant, the facts concerning maternal mortality are briefly presented. In 1915, for every 200 live births a mother's life was lost. Maternal deaths continued at this high rate for the next 20 years. It was not until after a concerted interest in the problem was aroused in 1932 and a program for curbing maternal deaths was begun that rates began to fall. In these years, the New York Academy of Medicine, in cooperation with certain voluntary agencies and the Health Department, undertook a study of maternal deaths.[1] It was concluded that two-thirds of maternal deaths were preventable and that, therefore, a reduction to 17 deaths per 10,000 live births would be an irreducible minimum. Maternal mortality committees which are still active were set up in each county of the city to review and investigate all maternal deaths with the aim of eliminating avoidable and unnecessary deaths. Obviously, better obstetrics, wider use of blood transfusions, and the discovery of antibiotics all played a role in the decline in maternal mortality which followed.

By 1945 the so-called irreducible minimum had been reached; only 17 mothers for every 10,000 live births were lost. Within a decade (1955) the rate dropped to 5 per 10,000, representing a 70% decrease below this irreducible minimum. It is reasonable to believe that even now the minimum has not been reached, since the cause of death is still in many instances a preventable one. It must be reemphasized that the mortality or condition of the mother is closely linked to the baby's survival too.

Infant and Fetal Mortality

Infant Mortality.—Again glancing back to the year 1915, we see an appalling loss of babies in the first year of life—for every 10 babies born alive then, 1 would die. Many of these deaths were needless, particularly those due to diarrhea and infection. These causes of death have largely been eliminated, with a resultant decrease in infant deaths postneonatally, i. e., after the first month of life. The cooperative efforts of doctors, health officials, and public-spirited citizens, resulting in a safe milk supply, improved sanitation, and education of the public in the fundamentals of hygiene and baby care, as well as the improved medical care of sick infants, were responsible for continuing improvements.

But there is little cause for complacency. From 1945 to 1955 the infant mortality rate in New York City dropped only 16%, from a rate of 31 per 1,000 live births to 25.8, and, as is readily seen in figure 1, has tended to level off. Maternal mortality in this same period dropped 70%.

Infant deaths viewed according to age at death may be divided into two groups—deaths of infants in the neonatal period (under 28 days) and those in the postneonatal period (28 days to one year). Deaths in the neonatal period now comprise three-fourths of all infant deaths, and of these neonatal deaths 90% occur in the first week of life (fig. 2). Approximately four-fifths of the deaths in the first week of life are due to causes associated with birth itself, namely, immaturity, 37%, anoxia and conditions of abnormal pulmonary ventilation, 26%, and birth injuries, 10% (fig. 3). Progress in reducing neonatal deaths, particularly those occurring in the first week of life, has been slight. As is well recognized, the reduction of infant mortality is due to gains made in saving the lives of those who live at least one month.

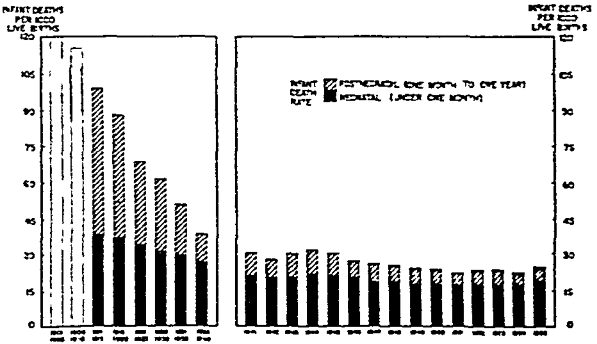

Fig. 1.—Infant mortality rate in New York City, 1901-1955 (neonatal data not available prior to 1911).

Fetal Mortality.—It is helpful to break down fetal deaths into three groups, depending on length of gestation, i. e., 28 weeks and over, 20 through 27 weeks, and under 20 weeks. The first two groups, i. e., late and intermediate fetal deaths, are quite completely reported in New York City. For the six years from 1949 through 1954, deaths of fetuses of 28 weeks' gestation and over decreased from 16.4 per 1,000 live births to 14.1 per 1,000—a drop of 14%. In the group of combined late and intermediate fetal deaths, those at 20 weeks' gestation and over, the reduction was only 8% (from 25.2 per 1,000 live births to 23.0 per 1,000 live births). For deaths of fetuses of under 20 weeks' gestation, we have noted a rapid rise in the ratio through the years. Better and more accurate reporting of deaths in this group undoubtedly accounts for this increase. Even now, reporting of fetal deaths is far from complete in this group of early fetal deaths.[2] In 1955, the total fetal death ratio was 123 for every 1,000 live births. The losses associated with deaths of viable and previable fetuses thus represent an enormous wastage of life.

Perinatal Mortality

As pointed out earlier, it is important to consider all the deaths closely associated with birth as a unit. Perinatal mortality, as routinely defined in New York City, is the combination of late fetal deaths (gestation of 28 weeks and over) and deaths occurring at time of delivery and in the first seven days of life. (The perinatal mortality rate is determined by multiplying this sum by 1,000 and dividing by total live births plus fetal deaths.)

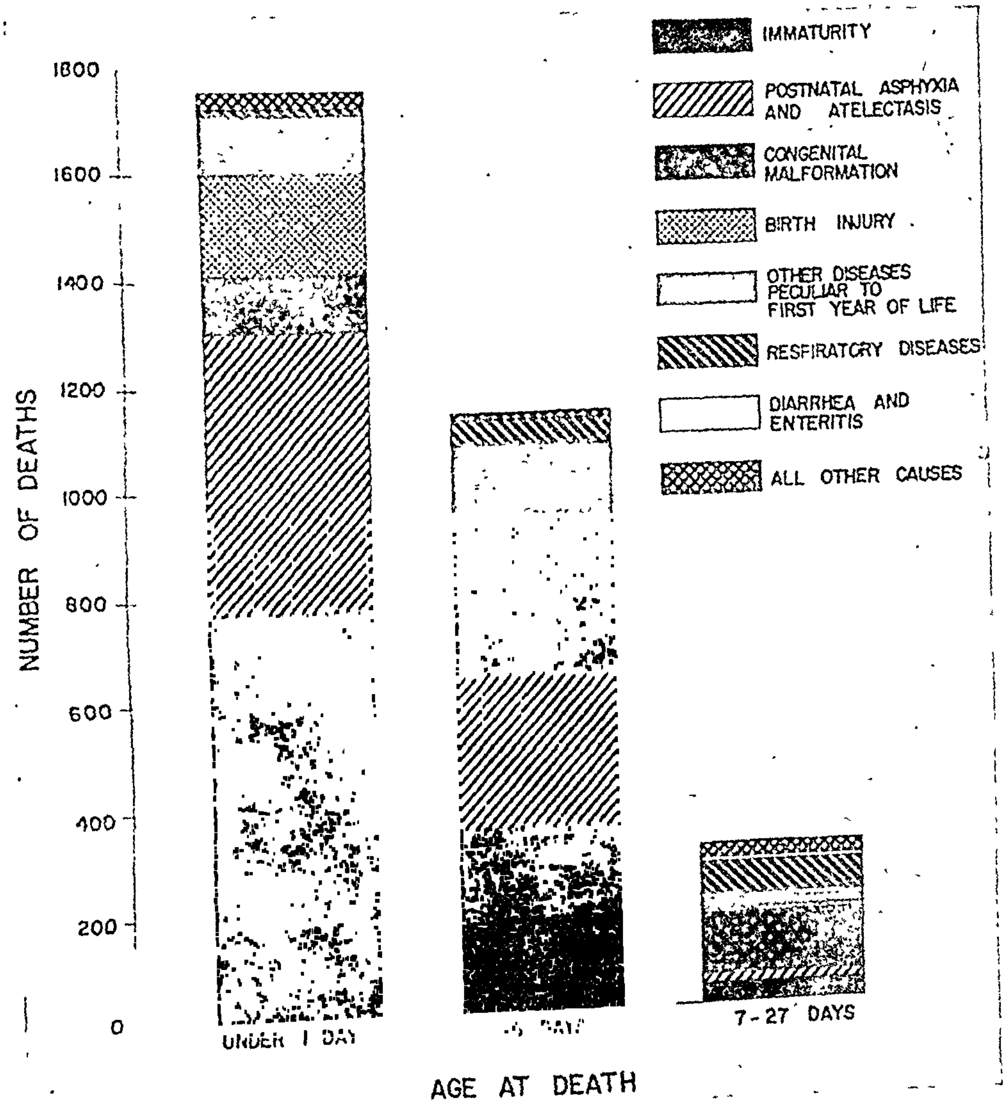

Fig. 2.—Neonatal mortality, by age and cause of death, in New York City, 1955.

Since 1949, progress in reducing perinatal deaths has been slow. There are slight variations from year to year. The perinatal mortality rates showed an 8.5% decrease from 32.6 in 1949 to 29.8 in 1954. However, in 1955 it rose again to 30.8 (table 1). In this same year, a rise occurred both in the neonatal and postneonatal periods for both white and nonwhite groups. These rises were statistically significant compared with the previous year, with the infant death rate rising from 23.7 to 25.8 and the neonatal mortality rate from 18 to 19.8. In the same year, 1955, the incidence of prematurity also showed a statistically significant rise from 8.8% to 9.4%. On the other hand, the late fetal deaths or stillbirth rate exhibited a slight decrease. This might mean that more of these fetuses were born alive and were augmenting the ranks of the prematurely born, poor-risk babies dying in the first week of life. This phenomenon one of us and a co-worker pointed out many years ago.[3] The average perinatal death rate for 1949 through 1955 is 30.6 (fig. 4). In short, there has not been great progress in curbing deaths associated with childbearing in the past five years.

A striking correlation exists between high incidence of prematurity, high perinatal death rates, and high incidence of late and no prenatal care. These, in turn, are associated with socioeconomic factors. Hospitals caring mainly for the lower socioeconomic groups had a high incidence of prematurity and a high perinatal death rate.[4] Conversely, hospitals catering only to private patients had a comparatively low incidence of prematurity and a low perinatal death rate (fig. 5). Furthermore, out-of-wedlock births are associated with higher fetal and infant death rates, higher incidence of prematurity, and higher incidence of late or no prenatal care. Out-of-wedlock births appear to be on the increase in the city and have been estimated conservately at 5.5% of all births.

The past five years in New York City have witnessed sustained high birth rates as well as population shifts. Since 1951, increasing proportions of births have occurred in nonwhite and in Puerto Rican groups and a decreasing proportion in white groups other than Puerto Rican. Births were 8% fewer in white groups (exclusive of Puerto Rican) but 15% more in nonwhite and 73% more in Puerto Rican groups (table 2). Since the nonwhite and Puerto Rican population in New York City is to a great extent confined to the lower socioeconomic groups, it is not surprising that a higher incidence of prematurity and higher perinatal death rates are found among these groups. In 1955, 165,150 births occurred, with a noticeable increase in general service cases from 32.3% in 1951 to 35.7% in 1955 (fig. 6). A higher incidence of deliveries was noted also for women receiving late or no prenatal care, with a rise in this group from 10.6% in 1951 to 15.6% in 1955.

The relationship of the socioeconomic factors to perinatal mortality can be demonstrated in other ways. For administrative purposes, New York City is divided into 30 health districts and each, in turn, is divided into health areas. A wide variation exists among these in incidence of prematurity, percentage of deliveries to women receiving late or no prenatal care, and fetal and infant death rates. The correlations are quite consistent. The districts heavily weighted with a lower socioeconomic population have the high mortality rates. The wide differences which exist are seen in table 3, and districts are further compared in table 4. In terms of preventable deaths, for 1955 alone it is estimated that 1,745 babies additionally could have lived if the rate of the most favorable district had prevailed city-wide. This is a conservative estimate, for preventable fetal deaths are not included.

The municipal hospitals which care for the lowest socioeconomic groups have the highest perinatal rates, 49.3, while the proprietary hospitals, caring only for private, paying patients, show the lowest perinatal rates, 22.6 (fig. 5). The quality of care in a given hospital cannot be judged solely by its perinatal mortality rate, which appears to be greatly influenced by the socioeconomic level of the population served. For this reason, we are presently grouping hospitals according to the type of patient cared for. Within a given category of hospital, a range of perinatal mortality is exhibited. It is only then that comparisons with a degree of validity can be drawn.[4] The size of the hospital may also influence the degree of variation in a rate—a small hospital obviously may experience a fluctuation in rate which may not be statistically significant because of small numbers, while the same fluctuation in a large hospital service may well be statistically significant. Since 1949, the perinatal rates in each category of hospital have shown a slight downward trend.

One can obviously view these data concerning perinatal mortality from the point of view of population changes. The failure to reduce infant mortality may then be attributed in New York City to changes in population composition, as we have shown, for there are greater proportions of births in these groups associated with higher mortality. However, that is not the real issue. To prevent mortality and morbidity in the less-favored socioeconomic groups is the real challenge. What else do we know of these losses? What has been done to curb them? What needs to be done?

Prematurity

The definition of prematurity used is that established by the World Health Organization in 1948, i. e., a weight at birth of 5.5 lb. (2,500 Gm.) or less.

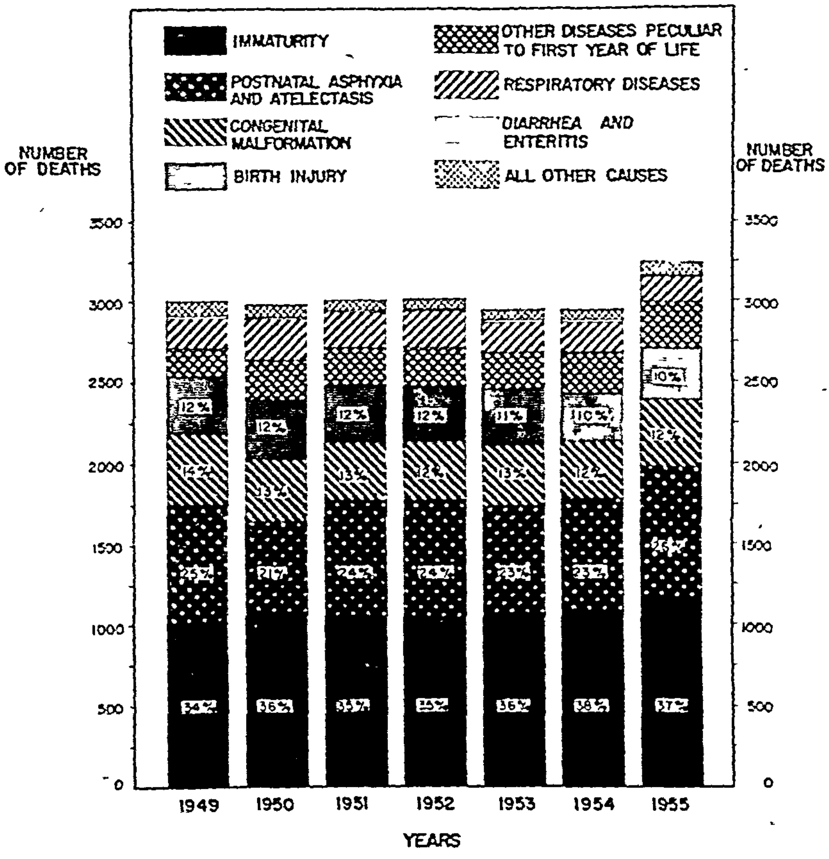

Fig. 3.—Neonatal deaths, by cause, in New York City, 1949-1955.

Since more than half of the early infant deaths occur in babies born prematurely, it is apparent that prematurity is a major cause of loss. Realizing its importance, the New York City Health Department 20 years ago spearheaded the development of a city-wide program for better care for the prematurely born infant. Since 1948, a complete program has been in operation[5]: a service picks the baby up in the home or hospital (when the hospital is not well equipped or staffed to take care of small premature infants) and transports him to a hospital which has a nursery that is specially equipped and staffed to care for such infants. He is transported in an incubator in a specially designed ambulance, with every precaution to guard his safety and well-being, under the watchful eye of a specially trained public health nurse. He is followed up in his home after discharge. High standards of medical and nursery care are maintained in centers for premature infants where special care, nursing, and medical and social services are available for these small premature babies. When families cannot meet all the costs of care, the difference is made up so that there are no financial barriers to procuring the best care available.

Table 1.—*Perinatal Mortality Rates, Fetal Death Ratios, and Hebdomadal Death Rates, per 1,000 Deliveries, New York City, 1937-1955*

	Perinatal Mortality Rate*	Fetal Death Ratio†	Hebdomadal Death Rate‡
1937	45.3	26.3	20.2
1938	45.4	26.4	20.2
1939	43.2	23.9	20.3
1940	43.4	23.6	20.8
1941	41.4	23.3	19.1
1942	39.3	21.8	18.3
1943	38.2	20.9	18.1
1944	38.7	21.1	18.5
1945	37.9	20.2	18.5
1946	36.9	19.3	18.4
1947	34.5	17.9	17.3
1948	34.1	17.1	17.5
1949	32.6	16.4	16.7
1950	31.0	14.9	16.5
1951	30.5	14.8	16.1
1952	30.7	14.9	16.3
1953	29.7	13.9	16.2
1954	29.8	14.1	16.0
1955	30.8	13.5	17.7

* Deaths under 7 days + fetal deaths of 28 or more weeks' gestation × 1,000 ÷ total live births + fetal deaths of 28 or more weeks' gestation.

† Fetal deaths of 28 or more weeks' gestation × 1,000 ÷ total live births.

‡ Deaths under 7 days × 1,000 ÷ total live births.

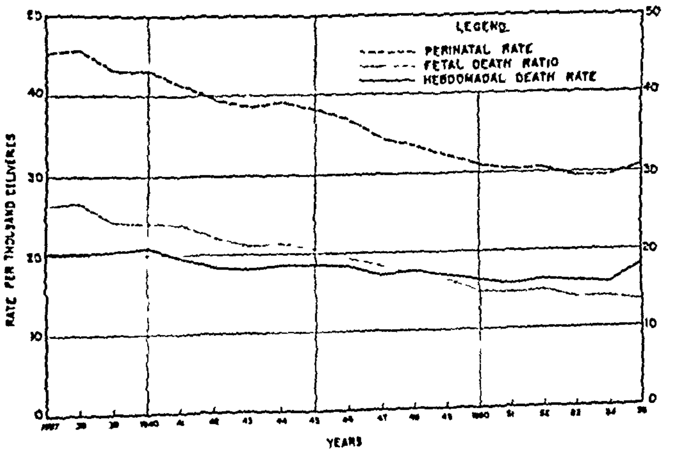

Fig. 4.—Perinatal mortality rate, fetal death ratio, and hebdomadal death rate in New York City, 1937-1955.

However, because existing centers are not able to meet all the demands, some babies are still deprived of this specialized care. It is figured conservatively that, in 1955, at least 550 more lives could have been saved if all babies had received the quality of care given in centers.

There is no question that the program for premature infants in New York City has paid dividends in saving lives, but what of the premature baby who survives the first month? What are his chances, compared to those of his full-term brother? The death rate in the postneonatal period of the prematurely born infant has shown no appreciable decline. In the smallest weight category, i. e., under 1,001 Gm. (2.25 lb.), the postneonatal mortality rate of the premature infant is 14 times greater than that of the full-term infant, in the 1,001 to 1,500-Gm. (2.25 to 3.25-lb.) group 10 times greater, in the 1,501-2,000-Gm. (3.25 to 4.25-lb.) group five times greater, and in the 2,001 to 2,500-Gm. (4.25 to 5.5-lb.) group, the most favorable weight group of premature infants, it is still 3 to 4 times greater than in the full-term baby.[6]

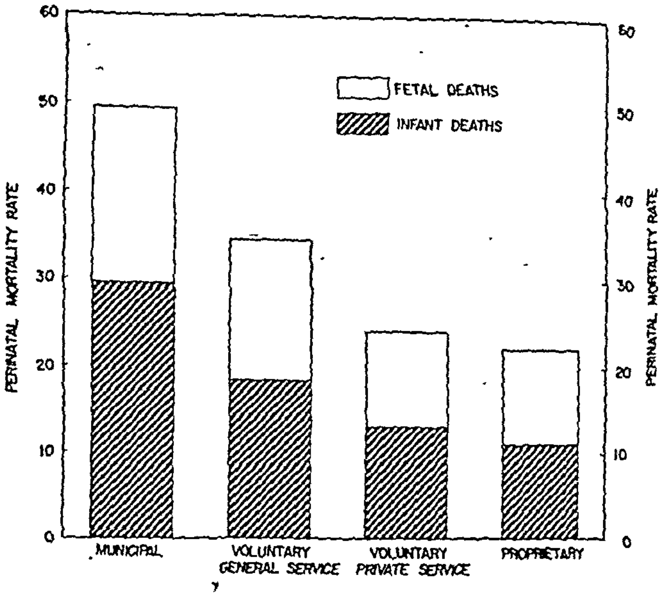

Fig. 5.—Perinatal mortality rate, by type of hospital and service, in New York City, 1955.

Intensive study of the factors contributing to these high postneonatal mortality rates is needed if improvement is to be effected. More careful and continued follow-up of the prematurely born infant after discharge from the hospital is essential. This aspect of the program for premature infants needs further strengthening, in addition to the expansion of premature centers to the needed capacity, so that no request for transfer of a premature baby need be denied.

Table 2.—*Live Births, by Ethnic Group, in New York City, 1950-1955*

		Puerto Rican		Other White		Nonwhite	
	Total	No.	%	No.	%	No.	%
1950	155,818	9,206	5.9	124,667	80.0	21,945	14.1
1951	162,755	10,479	6.4	129,096	79.3	23,180	14.3
1952	164,165	12,215	7.4	128,653	78.4	23,297	14.2
1953	161,499	14.431	8.9	123,093	76.2	23,975	14.9
1954	164,060	16.891	10.3	121,704	74.2	25.465	15.5
1955	165,150	18,365	11.1	119,692	72.5	27,093	16.4

The incidence of prematurity has also been found to be significantly higher in women who receive late and no prenatal care and in the unwed, both in our experience and in that of others. An increasing percentage of births in New York City is occurring in these less-favored groups. We do not know precisely how socioeconomic factors work. The nutritional status of the mother is of some importance.

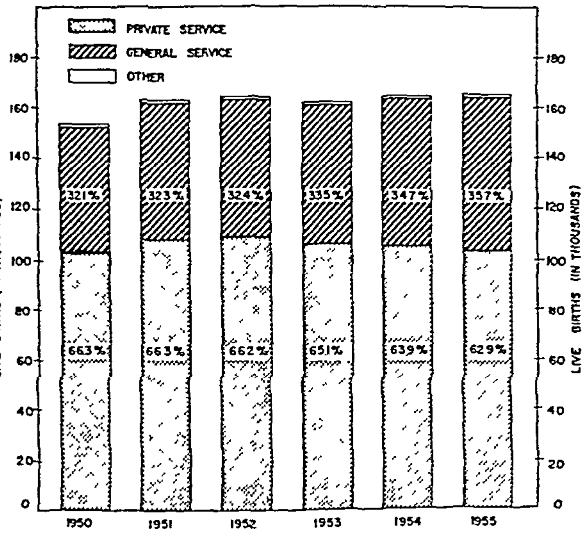

Fig. 6.—Live births, by type of service, in New York City, 1950-1955.

Of course, babies born to economically underprivileged Negro and Puerto Rican women tend to be smaller at birth and, though "full term," as judged by the length of gestation, may weigh 2,500 Gm. or less. The mortality rate of these "term infants" is higher than that of term infants weighing over 2,500 Gm.

What about the prevention of prematurity? Obviously, the basic difficulty is that so little advance has been made in knowledge of how to prevent premature labor and premature birth. Judging by the data on birth weights, no gains have been made in curbing premature births. In 1948, of the babies born alive in the city 8.8% weighed 2,500 Gm. or less. This percentage has been maintained in the years that followed and, in fact, rose to 9.2% in 1955, an increase which is statistically significant. Possible reasons for the failure to effect a diminution in premature births are indicated in certain associations, readily demonstrated in our figures. The drop in number of late fetal deaths, representing a possible carry-over into the liveborn premature group, has been mentioned. A higher incidence of prematurity, as judged by weight, occurs in the nonwhite or Puerto Rican groups as compared with the white, in the patients delivered on ward service as compared with private patients, and in the lower socioeconomic groups as compared with the upper socioeconomic groups.

These scattered epidemiologic observations and the few known clinical observations made on factors increasing the probability of premature labor do not yet furnish an adequate base of understanding of the mechanisms through which early labor is precipitated. Further elucidation is desperately needed. Common sense demands an enlarged and coordinated research attack on these fundamental problems.

Preventability of Perinatal Deaths

There is evidence that many perinatal deaths occurring today are preventable. This was clearly the conclusion of the study of a sample of the perinatal deaths made in 1950 and recently published by the New York Academy of Medicine.[7] This study, initiated at the suggestion of the Department of Health, was made with the cooperation of all hospitals and medical societies. On the basis of the careful analyses made, it was concluded that 35% of the perinatal deaths were preventable. The "pre-

Table 3.—*Perinatal Mortality Rates, Percentage of Live Births on General Service, Incidence of Prematurity, and Percentage of Live Births with Late or No Prenatal Care, New York City, 1955*

Geographic Area	Perinatal Mortality Rate*	% of Total Births: Delivered on General Service†	Weighing Less Than 2,501 Gm.	No or Late Prenatal Care‡
New York City, total	30.8	35.7	9.0	15.7
Manhattan, total	40.3	65.2	11.8	25.9
Central Harlem	51.1	92.4	16.3	39.5
East Harlem	34.9	78.4	10.7	29.4
Kips Bay-Yorkville	38.2	33.1	8.8	11.2
Lower East Side	32.7	55.2	10.1	21.7
Lower West Side	42.5	61.0	11.7	24.9
Riverside	42.3	65.7	12.4	29.4
Washington Heights	36.4	46.9	10.0	13.7
Bronx, total	30.3	39.0	9.0	13.6
Fordham-Riverdale	23.2	13.5	7.7	5.5
Morrisania	36.7	62.8	10.9	21.8
Mott Haven	39.0	66.8	10.1	21.8
Pelham Bay	24.1	19.4	7.4	6.9
Tremont	24.1	29.0	8.6	10.3
Westchester	28.4	20.3	7.5	7.7
Brooklyn, total	31.1	35.3	9.0	16.9
Bay Ridge	21.5	10.7	6.5	8.6
Bedford	41.1	66.2	13.1	26.5
Brownsville	35.8	25.0	9.0	18.6
Bushwick	30.3	33.2	8.3	16.9
Flatbush	25.3	8.6	7.6	8.6
Fort Greene	36.9	65.6	11.8	25.9
Gravesend	24.7	15.2	7.4	11.3
Red Hook-Gowanus	32.8	54.5	8.3	18.1
Sunset Park	27.7	24.3	7.0	11.0
Williamsburg-Greenpoint	34.3	48.0	9.4	24.7
Queens, total	21.9	15.6	7.5	8.7
Astoria-L. I. C.	25.4	20.7	6.8	9.1
Corona	24.9	16.5	7.5	8.6
Flushing	22.2	7.6	7.2	5.6
Jamaica East	28.7	29.0	8.7	14.3
Jamaica West	28.0	17.7	7.6	10.4
Maspeth-Forest Hills	21.0	5.6	7.4	5.0
Richmond	20.2	15.0	7.6	7.6

* Deaths under 7 days ÷ fetal deaths of 28 or more weeks' gestation × 1,000 ÷ total live births — fetal deaths of 28 or more weeks' gestation.

† Ward (nonprivate) service

‡ Prenatal visit first made in 3rd trimester.

ventability" rates were consistently higher for deaths in ward-service cases than for deaths in private cases, as well as in mature babies compared with premature. They were also higher in nonteaching hospitals.

Hospital Care.—Conditions in some hospitals have long been found to be not conducive to the best care for mother and child.[6] In recent years there has been a marked improvement. This is clearly shown in the regular reports made by the hospital consultation teams composed of an obstetrician, a pediatrician, and a nurse under the aegis of the health department. These teams visit all hospitals with maternity services and confer with the hospital staff. A high standard for maternity and newborn infant care has been set by a section of the Sanitary Code, which has the force of law. In the past five years, physical conditions in the inpatient service have been much improved. Blood is now readily available for transfusions. Physical conditions and equipment are much improved. und consultation policies are now in effect in the ajority of hospitals and have been considerably strengthened. The responsible directors of obstetric and of newborn infant services in hospitals are well qualified for their jobs and are, for the most part, in active charge of their respective services.

Just as the New York Academy of Medicine's study on maternal mortality in New York City in 1933[1] led to the formation of maternal mortality committees who reviewed all maternal deaths with the aim of calling attention to avoidable and needless mortality, the more recent study on perinatal mortality has stimulated the formation of perinatal mortality committees in the medical societies. Further, in many hospitals organized perinatal mortality conferences are now established in which the obstetric, pediatric, pathology, anesthesiology, and other related services participate. Much benefit is bound to accrue when the combined efforts and interest of the various groups are focused on a common aim of increasing knowledge concerning causes of death and preventing needless loss.

TABLE 4.—*Comparison of Districts with High and Low Perinatal Mortality Rates* and Selected Birth Characteristics, New York City, 1955*

	High Perinatal Mortality Rates					Low Perinatal Mortality Rates			
District	Perinatal Rate†	General Service,‡ %	Prematurity,§ %	Late or No Prenatal Care,‖ %	District	Perinatal Rate†	General Service,‡ %	Prematurity,§ %	Late or No Prenatal Care,‖ %
Total	30.8	35.7	9.0	15.7	Total	30.8	35.7	9.0	15.7
Central Harlem	51.1	92.4	16.3	39.5	Maspeth-Forest Hills	21.0	5.6	7.4	5.0
Lower West Side	42.5	61.0	11.7	24.9	Bay Ridge	21.5	10.7	6.5	8.6
Riverside	42.3	65.7	12.4	29.4	Flushing	22.2	7.6	7.2	5.6
Bedford	41.1	66.2	13.1	26.5	Fordham-Riverdale	23.2	13.5	7.7	5.5
Mott Haven	39.0	66.8	10.1	21.8	Pelham Bay	24.1	19.4	7.4	6.9

* Five districts with highest and five with lowest perinatal mortality rates.

† Deaths under 7 days + fetal deaths of 28 or more weeks' gestation × 1,000 ÷ total live births + fetal deaths of 28 or more weeks' gestation.

‡ Ward (nonprivate) service.

§ Weighing less than 2,501 Gm. at birth.

‖ Prenatal visit first made in 3rd trimester.

An important part of this picture is the traditional close cooperation of the official health and hospital departments with medical schools, medical societies, voluntary hospitals, and several hospital groups. The Department of Health leans heavily on advisory committees, composed of leading obstetricians and pediatricians. The policies and recommendations made by them are widely distributed and have considerable influence. The local association of hospital superintendents has been helpful, particularly in improving inpatient services.

Despite all of these advances, serious problems still exist in hospitals, the most important of which is shortage of staff members. How can the continuing problem of shortage of qualified nursing personnel be met? How can ancillary staff be provided and trained to assume some duties formerly assigned to regular nurses? Why should "preventability" rates be higher in ward-service patients than in private, in nonteaching hospitals than in teaching?[7] Qualified residents and interns are in short supply in a number of hospitals, especially in nonteaching hospitals. Medical schools and nurses' training schools must certainly be fostered and supported much more actively if standards of care are to be maintained—let alone advanced. New ways to use safely and effectively all kinds of more readily available ancillary personnel must be sought. Jobs must be analyzed so that precious professional time is not used for services given as effectively by those with less training. The patient should be added to the team. Providing safe anesthesia is still a problem in many hospitals.

Prenatal Care.—Prompt recognition, treatment, and prevention, wherever possible, of complications of pregnancy are of utmost importance for the welfare of the mother and the baby. The promotion of adequate and proper prenatal care is fundamental. It is disturbing to note that in New York City the incidence of late and no prenatal care has risen from 10.6% in 1951 to 15.7% in 1955 and that those districts where the highest incidence of prematurity and perinatal deaths prevailed are the ones with the highest incidence of late or no prenatal care (table 4).

What accounts for this lack of prenatal care in a city where obstetric, medical, and public health facilities are plentiful? Are services so unattractive that people will not use them? Do the younger, underprivileged women not realize the protection that comes from early and continuing medical supervision? What needs to be done?

For one thing, as one visits hospitals one gets the impression that the outpatient service is the stepchild of the obstetric service and that there is too little continuity of care between inpatient and outpatient service. Prenatal clinics are, in the main, overcrowded and understaffed, have too few physicians in attendance, and often lack adequate obstetric supervision. It is not uncommon to find no attending physician present for guidance and consultation.

Need for More Knowledge and More Accurate Diagnosis of Cause of Death.—The Academy of Medicine's study[7] of perinatal deaths pointed up the need for clarification and recording of causes of death, as well as the need for more and better pathological study. In this study, in only 35% of the babies had an autopsy been performed. In many autopsies, only partial examination had been made. The clinical and pathological diagnoses frequently did not coincide. City-wide figures have corroborated these findings for many years.

The leading causes of neonatal deaths, as now cited, are (1) immaturity (37%), (2) postnatal asphyxia and atelectasis (26%), (3) congenital malformations (12%), and (4) birth injuries (10%). Other diseases peculiar to first year of life, a "catch-all" category, accounted for about 8% (fig. 3).

The importance of postnatal asphyxia and atelectasis has led the infant mortality committees of the Medical Society of Kings County and now of New York County to devote time and thought to the prevention of asphyxia and atelectasis, as well as the resuscitation of the affected newborn infant. A comprehensive and most useful report on resuscitation of the newborn infant has been prepared by the New York County Infant Mortality Committee.[9]

Congenital Malformation

What of the infant born with a congenital malformation, birth injury, or cerebral palsy? Accurate knowledge of the incidence of these conditions could be greatly improved. We know that the reporting on birth certificates is not adequate. Frequently, recognition of the condition is not made until after the birth record has been filed. Ways and means of obtaining a more accurate picture of the incidence of these conditions must be explored, along with ways to assure more adequate rehabilitation of the victim.

Congenital malformations account for 12% of the neonatal deaths and 26% of the postneonatal deaths. Little is known of the factors operating in the causation of these aberrations in development or function.

The maternal complications which can lead to loss of life of the fetus or baby are those which, short of killing, can also handicap the infant. As an example, hemorrhage due to premature separation of the placenta or toxemia in the mother may create a state of oxygen deficiency in the fetus, resulting in premature birth, in death, or in brain damage. The association of rubella in early pregnancy with the incidence of congenital anomalies in the offspring is well established. Other viral diseases may be implicated as well. Detailed correlative studies of the complications of pregnancy in relation to the outcome of pregnancy should add to our scant knowledge of this subject.

Our data indicate that congenital malformations occur with greater frequency in the prematurely born infant as compared with the full-term infant.[10] Cerebral palsy is likewise more often associated with premature birth.

Since more children survive, those orthopedic and musculoskeletal deformities that are seen more commonly in the premature infant are becoming relatively more prevalent. The emergencies of "saving the life" of the infant sometimes mean that the physician who is not well trained in orthopedic abnormalities overlooks some deformities. There is a real need for early diagnosis and early case finding of such abnormalities. Training general practitioners, obstetricians, pediatricians, and nurses to recognize obvious orthopedic abnormalities is indicated. A delay of a few months in treatment in such conditions as congenital dislocation of hip may cause a permanent deformity which could have been prevented by early diagnosis and treatment.

What Lies Ahead

This, then, is the general picture of perinatal mortality in New York City. What lies ahead?

Research.—Obviously, with so large a proportion of the deaths in this age-period attributable to causes for which means of prevention are as yet unknown, an augmented and carefully balanced research program has high priority. The problems are social in nature, as well as medical. Research projects must utilize the skills of persons trained in different fields—obstetricians, pediatricians, sociologists, statisticians, geneticists, pathologists, anthropologists, nutritionists, physiologists, biochemists, and anatomists. Carefully planned, on-going longitudinal studies are of primary importance, because so much of our current knowledge is based on retrospective studies. For many years, the National Institutes of Health supported little research in this important field. It is to be hoped that the more recently established studies related to a better understanding of human reproduction will become an important part of the research programs financed by federal tax funds.

Aside from the basic research that needs to be done on the methods of preventing loss of life associated with pregnancy, there are practical "operational" research projects of one sort or another that will be useful. These should tackle such problems as finding ways to use existing personnel more effectively, ways to appeal to the woman who does not seek prenatal care, and ways to develop meaningful and acceptable preconceptual services.

Immediate Steps.—While we are waiting for better answers to these ancient problems, what specifically can professional and lay groups interested in reducing perinatal mortality do in New York City as of now? We have four suggestions to make.

First, the 15% of women now receiving late or no prenatal care under medical supervision should be seen early enough in pregnancy that they can benefit from that care. This will involve better methods of case-finding and better follow-up, and certainly the prenatal clinic must be brought "out of the basement," literally and figuratively. A new interest on the part of general practitioners, hospital superintendents, and obstetricians in prenatal care will do much to bring all pregnant women under prenatal care early in pregnancy.

Second, we need to strive for better teamwork the maternity services—better teamwork among general practitioners, obstetricians, pediatricians, nurses, ancillary workers of all kinds, and medical specialists of all kinds. The well-organized perinatal mortality conference in every hospital is a step in the right direction. Bringing the physiologist, pathologist, geneticist, sociologist, and nutritionist in at appropriate times may help. The orthopedist and the cardiologist, for instance, need to be brought in earlier to help with the handicapped baby. And, perhaps most important of all, letting the prospective parents themselves in on "the team" should bring rich rewards.

Third, New York City needs to complete the job of providing facilities for the prematurely born infant. This means putting into active operation all the beds located in currently approved centers for premature infants and developing the additional small numbers of centers that are needed.

Finally, we must pay special attention to the emergency problems created by the migration of so many underprivileged people into the city. This is not really a new problem. Every time there has been an immigration of people of lower socioeconomic groups, special efforts had to be made in their behalf. Infant mortality had always been high in this group—high until they got the kind of housing, jobs, medical care, and food they needed and until their language barriers were overcome. The help and interest of enlightened people in the community have always solved these problems. The basic question is this: Will we in the greatest and perhaps richest city in the world give economically underprivileged babies the same chance for life and health that other babies have?

125 Worth St. (13) (Dr. Baumgartner).

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DEATHS AROUND BIRTH—THE NATIONAL SCORE

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A comparison of the mortality figures for 1915 with those for 1955 shows that during this interval both maternal and infant mortality rates have been strikingly reduced. Maternal deaths have been reduced from 60 to 5 per 10,000 live births, and the infant mortality rate has dropped from 100 to 26 per 1,000. Further reduction is possible and necessary, for the frequency of perinatal and maternal losses was fourth among main causes of death at all ages in 1955 in the United States. The causes of perinatal mortality need to be identified because they must also be the causes of congenital handicaps in millions of infants who do not die. Differences in mortality between urban and rural patients and between different socioeconomic strata prove the importance of environmental factors. Preventing prematurity and improving the care of premature infants are among the immediate problems. For continued progress in the reduction of perinatal mortality it will be necessary to make sure that children who are to be the parents of the future grow up as members of healthy families in the best possible environment.

Death is associated with birth and being born in the United States more often than it is with any disease except heart disease, cancer, and cerebral hemorrhage. These deaths are among the most tragic, since they cut off life at its beginning or take a mother away from her family. In 1955, deaths in childbearing and being born numbered an estimated 165,376, of which 1,901 were maternal deaths, about 86,124 were deaths of infants before or during birth (if we take account of underreporting of such deaths), and 77,351 were deaths of liveborn infants in the neonatal period.[1]

Mortality, we know, is not the whole toll from sickness and misadventure in childbearing and being born. The aftermath for the mother may be chronic illness or repeated reproductive failure; for the infant, it may be irreparable damage, such as we see in children who suffer from cerebral palsy, epilepsy, mental retardation, and congenital malformations. In the United States today, mortality of the infant in the perinatal period, that is, in the period before, during, and soon after birth, is of vital concern to all who seek to conserve new life or who see in these fatalities a threat to continuing health in mothers and children.

Because there is much concern today with problems of maternal morbidity which result in premature delivery and with the causes of fetal and neonatal deaths, particularly those associated with congenital malformation, primary attention is given in this report to the whole perinatal period continuing to the end of the first month of postnatal life. The term perinatal mortality, as used here, embraces deaths of infants before or during birth (fetal death) in pregnancies of 20 weeks' duration or more and deaths of liveborn infants in the neonatal period (under 28 days), regardless of duration of the mother's pregnancy. This perinatal mortality rate is the number of such fetal and neonatal deaths per 1,000 births of live or stillborn infants. This rate is useful, since it helps us to view as a whole infant losses among mothers whose pregnancies are relatively advanced. Within this span, different intervals may be focused on separately, depending on the problem under study.

Perhaps at this point we should look back to see how far we have come in safeguarding mothers and babies during the maternity cycle and the first year of the infant's life. One of the reasons for the establishment of the Children's Bureau in 1912 was a nationwide concern about the deaths of infants and women during pregnancy and childbirth. At that time, the national score on infant and maternal mortality was not known. It was for this reason that one of the first activities of the young Children's Bureau was to work with the Bureau of the Census and the General Federation of Women's Clubs in establishing the birth registration area.

The first score was obtained in 1915. Although based on data from only a few states, it showed clearly that far too many mothers and babies were dying. For every 1,000 live births, six mothers died, and 100 infants, 1 out of 10, did not live to see their first birthday.

As we compare today's scores with those of 1915, we can feel considerable satisfaction in the accomplishments of the last four decades. Instead of six maternal deaths in 1,000 live births, now there are nearer five in 10,000. The infant mortality rate has dropped from 100 to 26 per 1,000. Seen in retrospect, the national score in 1955 looks extremely good.

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Read at the 57th Annual Meeting of the Association for the Aid of Crippled Children, New York, April 30, 1956.

Improved sanitation and standards of living, better nutrition, important discoveries in medicine, more and better hospital care and other health services—all these have contributed to this great saving of life. But, unfortunately, these benefits have not extended equally to all parts of the United States or to all groups of the population.

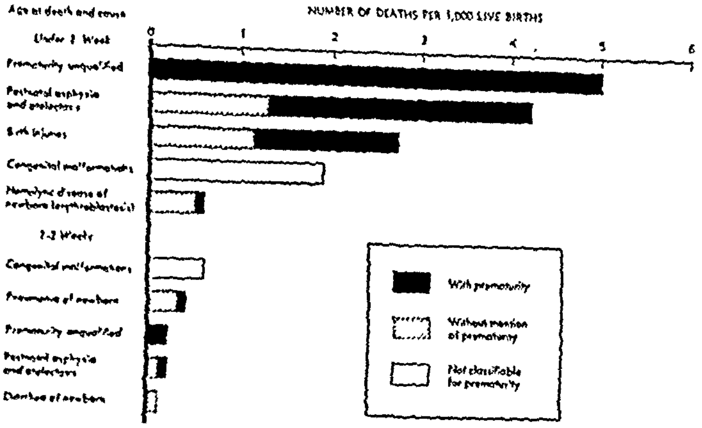

Fig. 1.—Early infant deaths by age and cause, United States, 1955 (data from National Office of Vital Statistics).

In many localities in the United States, progress in reducing infant and maternal mortality lags behind that for the country as a whole. For example, in isolated counties with no cities of 50,000 or more, the average annual infant mortality rate in the period 1951-1954 was 17% higher than that in counties with such cities.

Table 1.—*Neonatal Mortality Rate per 1,000 Live Births by Age and Main Causes of Death, United States, 1955**

Cause of Death†	Neonatal Death Rate‡ Total	Under 1 Wk.	1-3 Wk.
All causes	19.1	17.0	2.1
Certain diseases of early infancy.....760-76	15.4	14.2	1.2
With immaturity (.5)	11.4	10.8	0.6
Without mention of immaturity (.0)	4.0	3.4	0.6
Immaturity unqualified.....776	5.2	5.0	0.2
Postnatal asphyxia and atelectasis.....762	4.3	4.1	0.2
Birth injuries.....760-1	2.9	2.8	0.1
Pneumonia of newborn.....763	0.8	0.4	0.4
Hemolytic disease of newborn (erythroblastosis).....770	0.6	0.6	0.0
Neonatal disorders arising from maternal toxemia.....769	0.1	0.1	0.0
Hemorrhagic disease of newborn.....771	0.2	0.2	0.0
Diarrhea of newborn.....764	0.1	0.0	0.1
Other and ill-defined diseases of early infancy, including nutritional maladjustment 765-8, 772-4	1.2	1.0	0.2
Congenital malformations.....750-9	2.5	1.9	0.6
Influenza and pneumonia (except pneumonia of newborn).....480-93	0.0	0.0	0.0
All other diseases of respiratory system.....470-5, 500-27	0.3	0.3	0.0
All infective and parasitic diseases.....001-138	0.1	0.0	0.1
Gastritis, duodenitis, enteritis, and colitis (except diarrhea of newborn).....543, 571-2	0.0	0.0	0.0
Accidental mechanical suffocation in bed or cradle.....E924	0.0	0.0	0.0
All other accidental causes E800-923, E925-62	0.1	0.1	0.0
Other specified conditions.....Residual	0.4	0.3	0.1
Symptoms and ill-defined conditions.....780-95	0.3	0.2	0.1

* Exclusive of fetal deaths.
† Numbers refer to categories in 6th Revision of International List.
‡ Under 28 days.

Most of the reduction in the national infant mortality score has been due to a decrease in deaths after the first month of life. These have dropped from about 56 per 1,000 live births in 1915 to just over 7 in 1955. This saving of life has come about largely through the prevention and control of infectious and gastrointestinal disease.

But the death rate in the first month of life has dropped much more slowly. As we look at the principal causes of death in the neonatal period, we find that infectious and gastrointestinal disturbances are not important in the picture. The five main causes to which deaths in the first and later weeks of the neonatal period were attributed are illustrated in figure 1. Mortality rates for these and other causes in the neonatal period are shown in table 1. The causes are prematurity, postnatal asphyxia and atelectasis, birth injuries, congenital malformations, and hemolytic disease of the newborn, which results chiefly from Rh incompatibility. The conditions responsible for these early infant deaths nearly all have their origin before or during birth and are, for the most part, associated with morbidity in the mother.

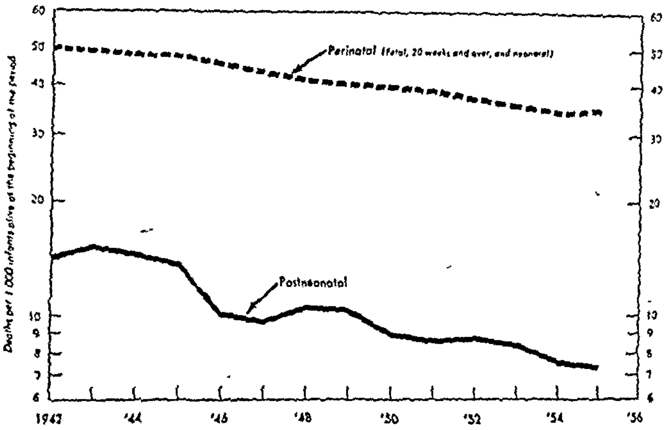

Fig. 2.—Reduction of perinatal death rate compared with that of postneonatal death rate, United States, 1942-1955 (data from National Office of Vital Statistics).

At least three out of five neonatal deaths are in infants whose mothers' pregnancies do not run to normal term. Although premature delivery is not usually thought of as evidence of maternal morbidity, surely some abnormality causes a mother to give birth before term. Premature delivery increases the risk of death in the newborn infant 20 times.[2]

The trend lines in figure 2 show the perinatal death rate and death rate for infants surviving the first month of life from 1942 to 1955. While the postneonatal mortality rate was cut in half, the perinatal mortality rate was reduced less than one-third. The perinatal death rate is now five times that of infants after the first month of life. In table 2 are given mortality rates for each of several intervals within the perinatal period and for the postneonatal period during these years. Each rate is based on the number of infants alive at the beginning of the particular interval.

An indication of the national importance of present perinatal and maternal losses can be seen in figure 3, where the frequency of such deaths is fourth among main causes at all ages in 1955 in the United States.

More and more evidence is accumulating that the same conditions that bring death to infants before, during, and soon after birth also may lead to chronic illness and handicap in many infants who survive. We do not know accurately how many children may suffer such results. But, from the limited information, a rough estimation is that probably 315,000 children have cerebral palsy,[3] 310,000 epilepsy, and 1,500,000 mental retardation. Something like 285,000 infants with congenital malformations are born each year (these estimations were made by the Children's Bureau to take into account underreporting).

TABLE 2.—*Perinatal Mortality Rates per 1,000 Infants to End of First Month of Postnatal Life and Infant Mortality Rate by Age, United States, 1942-1955*[*]

	Perinatal Period[†]					
			Neonatal Death Rate (Under 28 Days)[‖]			Post-Neonatal Period (1-11 Mo.)[¶]
	Total[‡]	Fetal Death Rate[§]	Total	Under 3 Days	3-27 Days	
1955	35.6	16.8	19.1	14.7	4.4	7.4
1954	35.9	17.2	19.1	14.4	4.7	7.6
1953	36.7	17.5	19.6	14.6	5.0	8.4
1952	37.4	18.0	19.8	14.8	5.1	8.8
1951	38.1	18.5	20.0	14.9	5.2	8.6
1950	39.0	18.8	20.5	15.3	5.3	8.9
1949	40.5	19.4	21.4	15.7	5.9	10.1
1948	41.9	20.2	22.2	16.1	6.2	10.1
1947	42.9	20.6	22.8	16.3	6.6	9.6
1946	45.8	22.3	24.0	17.1	7.1	10.0
1945	47.2	23.4	24.3	16.6	7.8	14.3
1944	48.0	23.9	24.7	16.8	8.0	15.5
1943	48.1	23.9	24.7	16.9	8.0	16.0
1942	50.0	25.0	25.7	17.7	8.1	15.1

[*] Deaths of live born infants in specified age group and deaths before or during birth (fetal deaths) of infants born to mothers pregnant 20 or more weeks, or duration unreported. In 1955, all states except Rhode Island required reporting of fetal deaths in pregnancies of 20 or more weeks' duration; Rhode Island required reporting at six completed months or more of pregnancy. For requirements by state in other years, see "Vital Statistics of United States," published annually by National Office of Vital Statistics.

[†] For unborn infant, beginning of perinatal period is coincident with or prior to onset of labor (or other termination of pregnancy).

[‡] Number of fetal and neonatal deaths per 1,000 births (live and still).

[§] Number of deaths before or during birth per 1,000 births (live and still).

[‖] Prior to 1949, neonatal period was under 30 days. Rate under 3 days of postnatal age is per 1,000 live births; for age groups 3-27 days, rate is per 1,000 infants surviving three days of postnatal life.

[¶] Number of deaths of infants 1-11 months of age per 1,000 surviving first month of postnatal life.

More research is needed to discover how such chronic illness and handicap are related to the 350,000 premature deliveries that occur to mothers of liveborn infants each year, to other complications of pregnancy, labor, and delivery, or to the diseases and defects that each year take an estimated 163,475 infant lives in the perinatal period.

The greatest hazards to the baby occur just before birth and during his first three days of life (fig. 4 and table 2). Since most of the babies who die soon after birth are born prematurely, our best chance to reduce deaths in these first few days lies in finding effective ways of insuring that the mother can carry her baby to term.

While fatal risks in the first 3 days of life have been cut very little since 1942 (17%), the neonatal death rate for infants surviving these days has been reduced 46% since 1942. No doubt this reflects, at least in part, improvement in the care of newborn infants, especially in the care of premature infants.

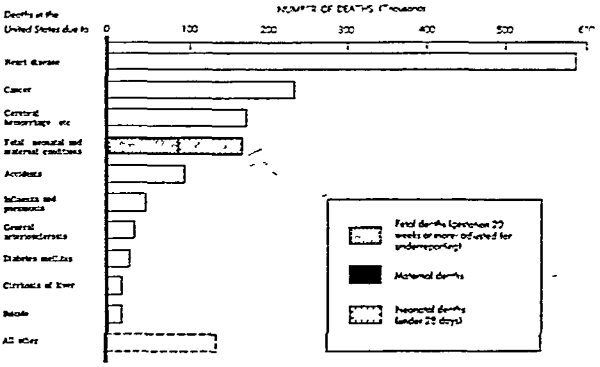

Fig. 3.—Comparison of fetal, neonatal, and maternal conditions causing death with other causes, United States, 1955 (data from National Office of Vital Statistics).

In recent years, more than half of the states and territories made some special effort in behalf of premature infants through their maternal and child health programs. Twenty-one were either supporting special services for premature infants or otherwise contributing to development of good hospital care for these infants. While much has been and is being done to improve care of such immature infants, much more remains to be done.

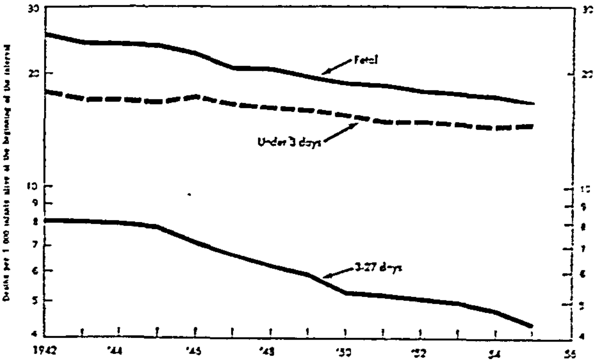

Fig. 4.—Reduction in deaths soon after birth compared with that for rest of perinatal period, United States, 1942-1955 (data from National Office of Vital Statistics).

Since 1942, the fetal death rate in the latter half of pregnancy has been reduced by nearly a third, from 25.0 to 16.8 per 1,000 births, live and still (see table 2). Presumably, this is the result of better prenatal and obstetric care of mothers. Mothers have a better chance today of giving birth to a living child than they had a decade ago. Some infants who formerly would have died in utero or during labor are born alive. Many of them survive, though some are too feeble for independent existence and die within a few days.

The volume of perinatal loss recorded in 1955 in the United States is shown in table 3 in relation to detailed age at neonatal death and duration of pregnancy in which fetal death occurred. Over half the neonatal deaths (52%) were on the first day of life; 89% occurred in the first week, 6% in the second, 3% in the third, and the remaining 2% in the last week of the neonatal period. Of the 69,153 fetal deaths recorded in 1955 in pregnancies of 20 or more weeks, 32% were in those reported as enduring 40 or more weeks.

How can we attack the problem of carrying infants safely through the perinatal period? Research is one answer. Not only do we need research to discover how various handicapping conditions of childhood are related to maternal and perinatal illness and defect but we also need knowledge of the whole chain of events underlying these conditions.

Table 3.—*Perinatal Mortality to End of First Month of Postnatal Life by Age at Neonatal Death, Duration of Pregnancies Resulting in Fetal Death, and Color, United States, 1955*[*]

Age at Neonatal Death, Days, and Duration of Pregnancy, Wk	Deaths, No.		
	Total	White	Nonwhite
Total perinatal period	146,504	113,751	32,753
Neonatal death (under 28 days)	77,351	61,340	16,011
<1 wk	68,654	55,140	13,514
<1 day	40,480	32,316	8,164
1 day	11,692	9,643	2,049
2 days	7,449	6,165	1,284
3 days	3,783	3,043	740
4 days	2,232	1,722	510
5 days	1,739	1,285	454
6 days	1,279	966	313
1 wk	4,374	3,196	1,178
2 wk	2,475	1,766	709
3 wk	1,848	1,238	610
Fetal death	69,153	52,411	16,742
20-27 wk	16,200	11,781	4,419
28-31 wk	8,557	6,299	2,258
32-35 wk	9,035	7,118	1,917
36-39 wk	13,187	10,485	2,702
40+	22,174	16,728	5,446

[*] Deaths of live-born infants in specified age groups and deaths before or during birth (fetal deaths) of infants born to mothers pregnant 20 or more weeks, or duration unreported.

Understanding the reproductive process calls for many different approaches. One approach, animal research, is producing important clues as to possible causes of congenital defects. We need many more such studies, together with studies showing the application of these findings to human beings.

Another approach lies in clinical and pathological studies of untoward conditions during pregnancy and follow-up studies of surviving infants. For example, what are the causal factors in bleeding in early pregnancy, and how does this affect the fetus? Or, what are the significant events associated with premature labor? True, we know some of them, but, for the majority, we can only guess. In a study at Johns Hopkins University of premature deliveries, no explanation could be found in 60% of the cases.[4]

The clinical and public health approaches to these problems can be combined in forward-looking studies of successive pregnancies from the beginning of each pregnancy through delivery with long-term and regular follow-up of the mother and her children. This is one way physicians can learn more about the immediate and long-run bearing of specific events in early pregnancy on the health of the mother and the development of her child. Studies of this sort are now being initiated in a number of clinics.

Obviously, research on reproduction calls for the knowledge and skills of many scientific disciplines: obsterics, pediatrics, pathology, chemistry, physiology, embryology, genetics, biostatistics, public health administration, and others.

Many investigators believe that, although each of these specialties has its own approach to these studies, all specialists can work more fruitfully if their efforts are coordinated. This does not necessarily mean coordination through formal plans and agreements, but, the kind of coordination that occurs from exchange of ideas and from joint thinking about the problem when different approaches intersect or overlap.

Of some things we are certain. We know that good care for infants born prematurely saves many who would not survive otherwise. Services to provide such care should be available wherever infants are born.

We recognize the need for more extensive and more effective maternal and child health services, especially in rural areas and for the less fortunate socioeconomic groups. But just what is meant by more effective services? For one thing, a program that accepts prenatal care as one of its major functions is necessary. An analysis of the way public health nurses use their time shows that 40% of it is devoted to maternal and child health, but, of this, only 10%—4% of the total time—is given to prenatal care.

More attention needs to be given to finding those expectant mothers who are less likely to seek care for themselves and who more often need intensive service. And we can give thought and study to how the nursing visit can be most meaningful.

Continuity in care throughout pregnancy and labor and the postpartum and interpregnancy periods is essential to the best maternity care. Commonly, continuity in medical care for the pregnant woman is provided by physicians in their private practice. The support and supervision thus given may be even greater if the plan of care provides also for visits to the family by a public health nurse. Often, however, when a mother seeks maternity care in a hospital or other clinic this continuity of medical care does not exist. She may be seen by more than one physician during a single pregnancy and be delivered by still another. Between pregnancies she may not be seen at all by either physician or nurse. Much attention needs to be given to this aspect of maternity care if premature delivery and perinatal mortality are to be reduced.

Studies of obstetric case histories usually reveal a certain proportion of women who have had repeated unsuccessful pregnancies. For a physician to dismiss such a woman after her postpartum examination may mean he is dismissing her at a time that she most needs study and treatment. By the time her next pregnancy is confirmed, it may be too late to do anything about helping her carry her baby to term.

In cases where a woman has had one or more unsuccessful pregnancies, careful diagnostic study of both husband and wife are indicated, with treatment as necessary, before another pregnancy occurs. The treatment may be psychological, nutritional, or physical, with endocrine therapy when needed. Such study and treatment are best carried out by a team—physicians, nurses, social workers, nutritionists, and psychologists—each member contributing an important share.

An aspect of prenatal care too often neglected is the provision of hospital care when complications of pregnancy occur. Where good hospital care is available, a woman with toxemia or threatened abortion can often be carried through until the infant becomes mature enough to have a good chance for survival. Or, if toxemia in later pregnancy is too severe, the premature induction of labor may prevent a fetal death, possibly even a maternal death.

A few state health departments now make funds available for hospitalization of women with complications of pregnancy. These funds can be used more effectively in a program which has a carefully developed referral system and nursing follow-up.

For another thing, we need services directed especially to the socioeconomic groups that are most vulnerable. In Denver, a study of the women admitted to the hospital because of complications of pregnancy showed that a large proportion came from an area of low socioeconomic development in which the general health level was low. At the University of Aberdeen, Scotland, where nearly all of the women received the same maternity care, premature birth and perinatal death were found more often in infants of mothers from the lower socioeconomic groups than they were in those of upper social groups.[5]

In the United States, we have evidence that perinatal mortality is affected by the socioeconomic status of the mother. Perinatal losses are higher for the nonwhite population than for the white; the fetal death rate is 85% higher among nonwhite mothers than among white, and the perinatal rate more than 67% higher than for white (table 4). While some of these differences reflect the younger age and larger families of nonwhite mothers, undoubtedly they also represent differences in economic status and deficiencies in early and present environment. Similarly, in the careful study on incidence of congenital malformations reported from Babies Hospital and Sloan Hospital for Women in New York City, a significantly higher incidence was found among nonwhite as compared with white infants.[6]

Summary

Today, the greatest loss of infant life occurs around the time of birth. Much of this fatality could be prevented if present knowledge were more widely and intensively applied. Medical, nursing, and hospital services should be more readily available outside of cities. Too few good hospital services exist for premature infants. Maternity services should seek out and give special attention to the woman who has already had an unsuccessful pregnancy when, or even before, she becomes pregnant again. Early environment may affect a woman's ability to bear children successfully. Consequently, we must concern ourselves with the nutrition and health of all of the family if little girls growing up today are to bear healthy babies tomorrow.

Table 4.—*Perinatal Mortality Rate to End of First Month of Postnatal Life by Color, United States, 1955*

	White	Nonwhite	Ratio	Total
Perinatal rate per 1,000 births (live and still)	32.4	54.1	100:167	35.6
Fetal rate per 1,000 births (live and still)	14.9	27.6	100:185	16.8
Neonatal rate (under 28 days) per 1,000 births (live)	17.7	27.2	100:154	19.1

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CHALLENGE OF FETAL LOSS, PREMATURITY, AND INFANT MORTALITY—A WORLD VIEW

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Comparison of data from various countries shows that large differences exist with respect to the loss of human life from premature births, deaths during the neonatal period, and deaths in the age period from one month to 4 years. Attention is called particularly to the very high death rates in the age group of 1 to 4 years in economically less developed areas. The differences are seen to be largely correctable. This is proved not only by contemporary comparisons of country with country but also by comparison of past with present mortality rates in countries where adequate records have been kept. Three phases of action are suggested to reduce this loss of human life: A first point of attack is to establish and strengthen basic public health services, including maternal and child health services, in economically less developed areas. A second is a series of specific measures to reduce prenatal and neonatal mortality, for instance, by improved prenatal care and by improved treatment of premature infants. A third is an intensive program of research aimed at the identification and correction of all factors that may handicap a child in either its intrauterine or its postnatal growth. The first measure is essential for the reduction of excessive mortality in the age period 1 month to 4 years. The second and third measures are increasingly important in the reduction of perinatal mortality.

In dealing with fetal loss, prematurity, and infant mortality on a world basis, it is advisable to consider this subject within the framework of the problem of mortality in childhood throughout the world. Although risk of death diminishes as children advance in age, in many areas of the world death rates are not only high in infancy but continue to be so in early childhood, becoming much lower only at school age. There is great variation between economically developed and less developed countries. Grouping the latter, which represent three-fifths of the population of the world, approximately 50% of all deaths are of children under 5 years of age, while in the technically advanced countries, including one-fifth of the world population, only 10% of the deaths are in this age group.[1]

Variation in Death Rates

The situation regarding mortality in infancy and early childhood is presented in figure 1, which shows death rates for children under 1 year and for those 1-4 years of age for 25 selected countries of the world (derived from the Demographic Year Book of the United Nations for years up to 1954, the Annual Epidemiological and Vital Statistics of the World Health Organization [WHO] for years up to 1952, and annual and special reports of these gencies and countries). There is an association be- en high rates and low economic development, attention is called particularly to the very high rates in the age group of 1 to 4 years in omically less developed areas.

order to focus attention on the problems of the present discussion, variations in fetal, neonatal, and postneonatal (1-11 months) death rates per 1,000 live births are shown for the same countries (fig. 2). The data are highly unequal in quality, particularly with regard to fetal loss and neonatal mortality. Here, differences are the result of gross incompleteness of registration in some countries in addition to the variation due to differences in definition of fetal deaths and live births. In spite of the inaccuracies, the variation in neonatal mortality in these 25 countries is substantially less than the variation in postneonatal mortality. Also, if accurate data could be obtained for fetal deaths, it is probable that differences would be similar to those noted in the neonatal period. The lesser variation seen in the neonatal period and assumed for the fetal period can be related to the fact that the external influences have less effect on the fetus and the newborn infant than on the child in the subsequent months of his life. Therefore, the greater variation seen in the postneonatal period is a reflection of the influence of the environment, and the marked decline in postneonatal mortality in the technically developed countries is the result of improved health conditions and, in general, of the improvement of socioeconomic conditions. Following the decline in infant mortality, due to the reduction of the causes of death in the postneonatal period, the problem of wastage of life becomes centered on birth in the

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From the Pan American Sanitary Bureau, Regional Office of the World Health Organization.

Read before the Annual Meeting of the Association for the Aid of Crippled Children, New York, April 30, 1956.

prenatal, natal, and neonatal period. Thus, in Chile, where the infant death rate is high, 51% of the wastage of life up to one year in 1952 occurred in the prenatal and neonatal period, while in Sweden 86% of the loss occurred in the same period.

To demonstrate changes over a period of time, fetal and infant death rates (fig. 3) are shown for three countries[2] over a period of nearly 40 years.

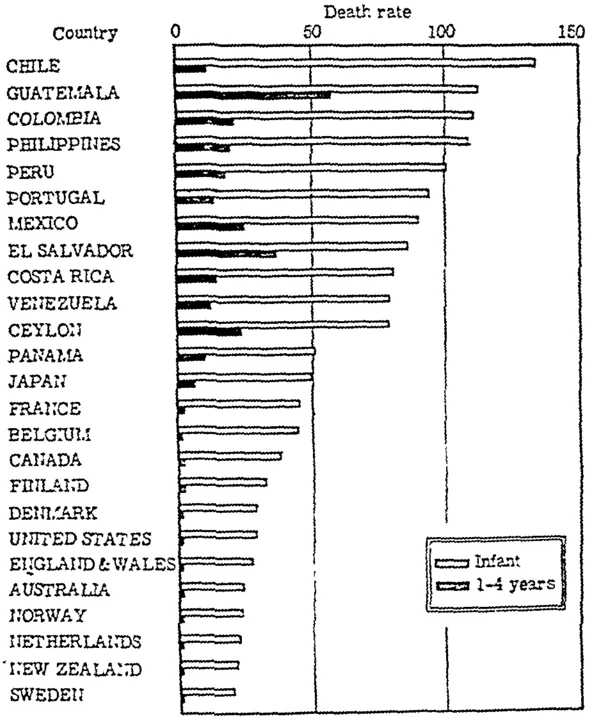
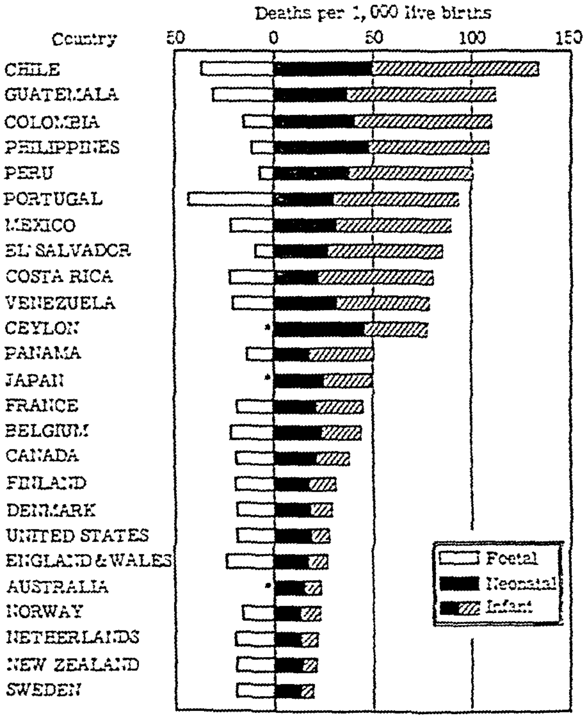


Fig. 1.—Infant deaths per 1,000 live births and deaths of children 1-4 years of age per 1,000 population for 25 selected countries, 1952.

The lower limits for registration of fetal deaths were as follows: in Sweden, fetuses no less than 35 cm. long; in the Netherlands, fetuses of at least 26 weeks' gestation before 1950, and, in 1950, 28 weeks' gestation and 35 cm. long; and, in the United States, 20 weeks' gestation. Rapid decline is evident in infant mortality and a slower decline in neonatal mortality and in fetal loss. Within the neonatal period the decline occurred mainly in the period of 1 through 3 weeks, whereas the death rate under one week has remained almost constant. The stability of mortality in the first week of life is further illustrated by the fact that, in the Netherlands in the last five months of World War II, the tremendous increase in infant mortality was only partially reflected in neonatal mortality and not in mortality of infants under one week of age.

The mortality in the prenatal period and soon after birth is commonly called perinatal mortality. The limits used for this mortality period vary at present and result in difficulties in analysis of data. We recognize that the causes determining this mortality are often interrelated and have their roots in circumstances early in the life of the mother, while they may also determine for the child increased hazards or handicaps for growth and development. Yet their direct impact on mortality is essentially measurable only within a limited period. In considering this problem, the WHO Study Group on Perinatal Mortality[3] expressed the desirability for uniformity and made the following statement: "It would seem that the age of practical viability, usually set at 28 weeks of gestation, could reasonably establish the lower limit, and since the majority of deaths in the neonatal period . . . occurs in the first week (a time when perinatal and natal influences still dominate and before the exogenous forces of such wide variance make their influence felt) the upper limit could be set at the end of the first week of life." These limits would provide data for a minimum period which, on a world basis, would have greater comparability than data for a more extended period. There is justification for this in the fact that late neonatal mortality (1-3 weeks) from exogenous causes is much greater when countries have high infant mortality. While in 1915 32% of the neonatal mortality in the United States and 44% in Sweden occurred after the first week of life, in 1952 the corresponding percentages were 13 for both countries.



* Not available

Fig. 2.—Fetal, neonatal, and infant deaths per 1,000 live births for 25 selected countries, 1952.

Variation in perinatal mortality and its relative importance in wastage of life is illustrated for six countries at different stages of development (table 1). These countries are selected for comparability of data, are those with registered fetal deaths having the lower limit of 28 weeks' gestation, termed "late fetal deaths,"[4] and are those in which deaths under 7 days were recorded. Their perinatal mortality rates vary from 27.1 to 63.4 per 1,000 total births. (The denominator recommended for the calculation of perinatal mortality is total births, which is the number of fetal deaths plus the number of live births.) Furthermore, mortality during this period was over 70% of the total loss in the fetal and infant periods in three countries (United Kingdom, the Netherlands, and Norway) and less than 40% in two countries (Chile and Costa Rica).

TABLE 1.—*Fetal, Perinatal, and Infant Death Rates for Six Countries, 1952*

Country	Fetal Deaths per 1,000 Total Births	Deaths Under 1 Wk. per 1,000 Total Births	Infant Deaths per 1,000 Live Births	Perinatal Deaths* per 1,000 Total Births	Perinatal Deaths* % of Total Fetal and Infant Deaths
Chile	35.9	27.5	133.6	63.4	38.5
Costa Rica	21.3	13.1	80.2	34.4	31.4
Canada	17.7	17.5	38.0	35.2	61.0
United Kingdom†	23.1	15.1	28.4	38.2	75.1
Norway	15.3	11.8	23.7	27.1	70.1
Netherlands	18.2	12.6	22.4	30.8	76.4

* Late fetal deaths and deaths under 1 week.
† Excluding Northern Ireland.

Causes of Mortality

In order to understand the underlying mechanisms that govern the reduction or lack of reduction of mortality, figures 4, 5, and 6 show data regarding the major groups of causes of deaths in infancy and childhood for selected countries. Death rates in the age roup of 1 to 4 years are very ow for the United States, Swen, and Australia in comparin with the three others, inditing the extreme reducibility f death rates in this period of life.

In the first year of life (fig. 5), mortality[1] is also greatly reduced in the same three countries but not to the same extent. The reduction in mortality in these two age groups is determined essentially by three major groups of causes, namely, digestive diseases, respiratory diseases, and infective and parasitic diseases. However, in infancy there is residual mortality, due to a group of causes—congenital malformations and diseases of early infancy—which has not been greatly reduced even in the three countries with low infant mortality. The data for neonatal mortality (fig. 6) have to be interpreted with great caution because in countries with limited medical facilities the quality of certification of causes of death is poor. For the three countries with high rates, the data for Venezuela are probably the most reliable, since the rates were estimated on the basis of the distribution of 47% of the deaths medically certified. The great divergencies in the two others reflect essentially the poor quality of certification. Nearly all of the deaths in this neonatal period are due to the group comprising congenital malformations and diseases of early infancy, particularly in the United States, England and Wales, and Australia. This group may be considered in four subdivisions, namely, congenital malformations, birth injuries, other diseases peculiar to early infancy and immaturity unqualified, and infections of the newborn infant. The low rates for Ceylon for infections of the newborn infant, birth injury, and congenital malformations probably indicate that these causes were not stated on certificates, thus enlarging the proportion assigned to the less specific group "other diseases of early infancy." Some of these causes of death, such as pneumonia and diarrhea of the newborn infant, are more readily preventable, but the majority of deaths in the countries with low rates are difficult to prevent because of the underlying influence of immaturity.

Data on causes of fetal deaths are often unsatisfactory. Certain causes, such as birth injury and congenital malformations, influence both fetal and neonatal mortality, pointing to the interrelationship of causation.

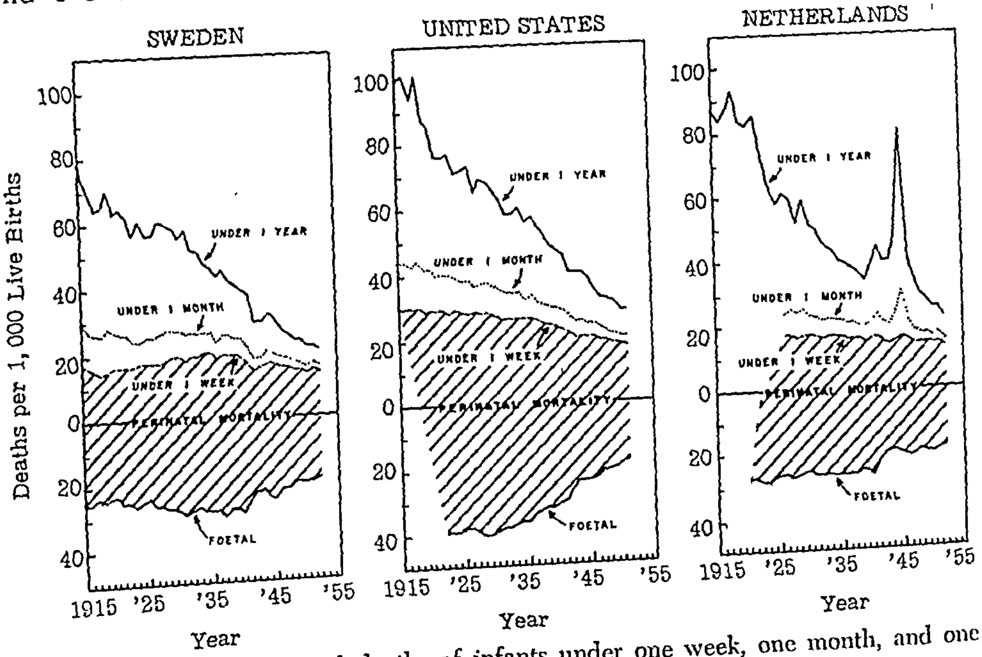


Fig. 3.—Fetal deaths and deaths of infants under one week, one month, and one year of age for Sweden, United States, and Netherlands, 1915-1952.

Analysis of data for Birmingham, England (table 2) shows, for instance, how certain causes play a role throughout the fetal and neonatal periods, while other specifically influence one period. Thus, toxemia and separation of the placenta influence mortality in both periods primarily in premature infants. On the other hand, intranatal causes—essentially, birth trauma—influence both the fetal and neonatal mortality principally in the mature infant.

Mortality and Birth Weight

The condition of the infant at the time of birth is greatly influenced by his maturity, and prematurity plays an important role in both fetal and neonatal deaths. Although length of gestation is the most accurate measure, the generally accepted and most practical measure of maturity is birth weight. It is, therefore, important to consider its distribution and variation. For a number of years, the differences in average birth weights were attributed primarily to innate host factors, such as race and sex of the child, and the variations by birth order, age of the mother, and plurality of births have been shown. In addition to the recognized innate differences, improved knowledge of environmental factors, such as social status, health of the mother, and nutrition, promotes increasing recognition.

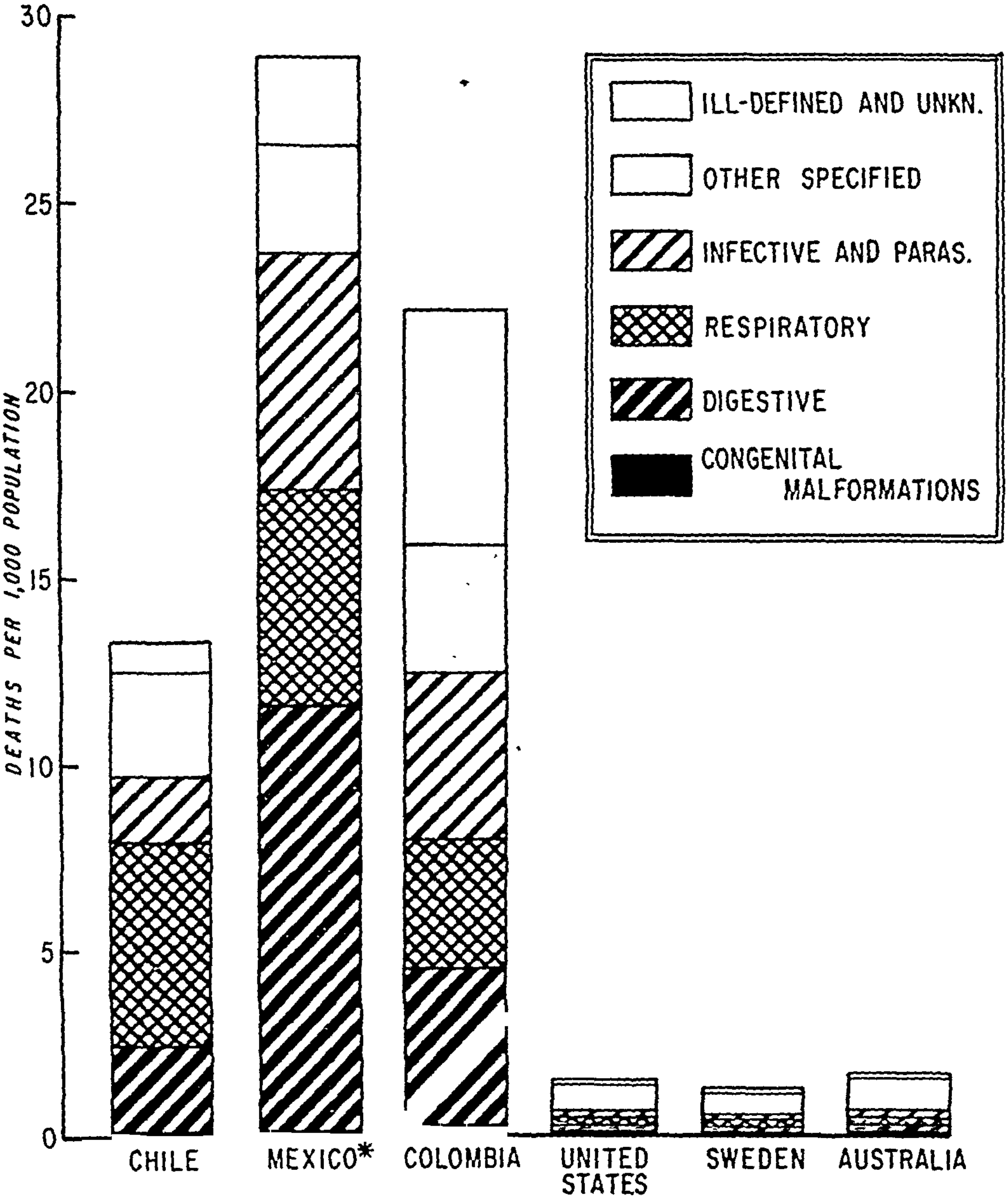


Fig. 4.—Deaths per 1,000 population by cause in age group 1-4 years for six selected countries, 1950-1952 average (for Mexico, calculation was based on 1950-1951 distribution of deaths).

Data regarding average weights of live births, collected from UN, WHO, and other reports, give a range of values from 2,760 to 3,500 Gm. (6 to 7.75 lb.). Caucasians show the highest birth weights regardless of geographic location (Netherlands, 3,500 Gm. (7.75 lb.) [6]; Birmingham, England, 3,280 Gm. (7.25 lb.) [5]; United States (white population), 3,320 Gm. (7.35 lb.); and South Africa (European population), 3,390 Gm. (7.5 lb.).[7] In contrast, average weights below 3,000 Gm. (6.75 lb.) are almost consistently found in the Bantu populations of South Africa,[8] and similar figures are recorded in India [9] and Ceylon.[10]

A more accurate picture of the variation of birth weights is shown by the distribution of live births by weight, as in figure 7. Data for the white population of the United States (from special reports of the National Office of Vital Statistics) and for Birmingham, England,[5] show the same general weight distribution. The other racial groups have a shift to the left, that is, to lower weights. The Bantu of South Africa [7] and the nonwhite population in the United States have higher percentages in the lower weight groups than do the Caucasians. The greatest shift to the left is shown by the Indians of South Africa[7] and of Calcutta.[9] (For the former group, data were collected from various hospitals and nursing homes in Durban, Pietermaritzburg, and Capetown. "Indian" is used to refer to persons from India or originating from India who have moved into the Union of South Africa. For the latter group, data were recorded in Ramkrishna Mission, Shishumangal Pratishthan, Calcutta, June, 1952, to February,1954.) These differences in the weight distribution curves greatly influence the frequency of prematurity, taking the birth weight of 2,500 Gm. (5.5 lb.) as its upper limit according to the accepted classification.[11] Thus, for the United States and Birmingham, England, the proportions below this dividing line were 7.0% and 7.4% respectively. For the nonwhite population in the United States, the percentage was 11.2 and for the Bantu in South Africa 11.6. The percentages increased for the Indian in South Africa to 18.3 and for the group in Calcutta to 34.7. Taking into account, in addition, the low percentages of 3.5 for the Netherlands,[6] 4.6 for Denmark,[6] and 5.4 for Oslo, Norway,[12] where the average birth weights are known to be higher, the range in the frequencies of prematurity is very great. This raises questions about the adequacy of the dividing line of 2,500 Gm. as the upper limit for prematurity for all populations throughout the world.

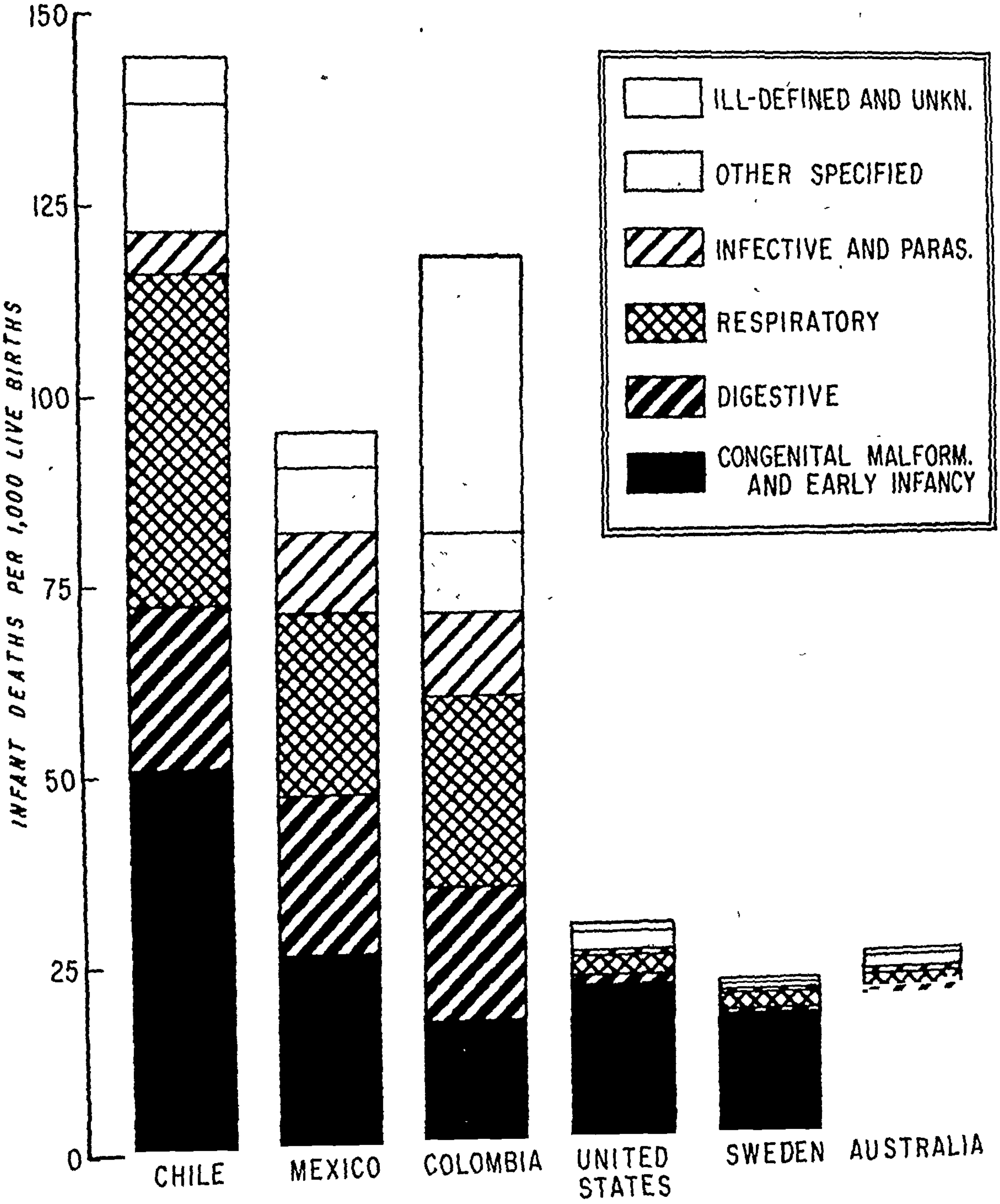


Fig. 5.—Infant deaths per 1,000 live births by cause for six selected countries, 1950-1952 average.

Analysis of mortality by birth weight groups provides further evidence regarding the problem of measurement of prematurity by weight. Mortality in the first week of life (data from the National Office of Vital Statistics and Chaudhuri[9]) is shown in table 3 for three weight groups in Calcutta and in the white and nonwhite population of the United States. In Calcutta, where 35% of the births in the study weighed 2,500 Gm. or less and, thus, the average birth weight was low, 9.1% of the premature infants died under one week of age. The percentages of the premature infants who died under one week of age were much higher for the white population (16.2%) and for the nonwhite population (14.2%) of the United States, where only 7% of the white and

10% of the nonwhite live births were premature by the same standard. The average birth weight of the white live births in the United States was 3,320 Gm. (7.35 lb.) and of the nonwhite 3,270 Gm. (7.25 lb.). Thus, these data indicate that mortality is more favorable for premature infants by this definition in experiences with lower average birth weights. This indicates that, in populations with substantially different birth weights, the single limit of 2,500 Gm. cannot be utilized to compare physiological performance. In a study in Baltimore[13] of Negro infants it was necessary that the limit be lowered to 2,320 Gm. (5.25 lb.) to obtain a mortality rate equivalent to that of white infants, and in Calcutta[9] it is suggested that a lower maturity weight, 2,270 Gm. (5 lb.) be used.

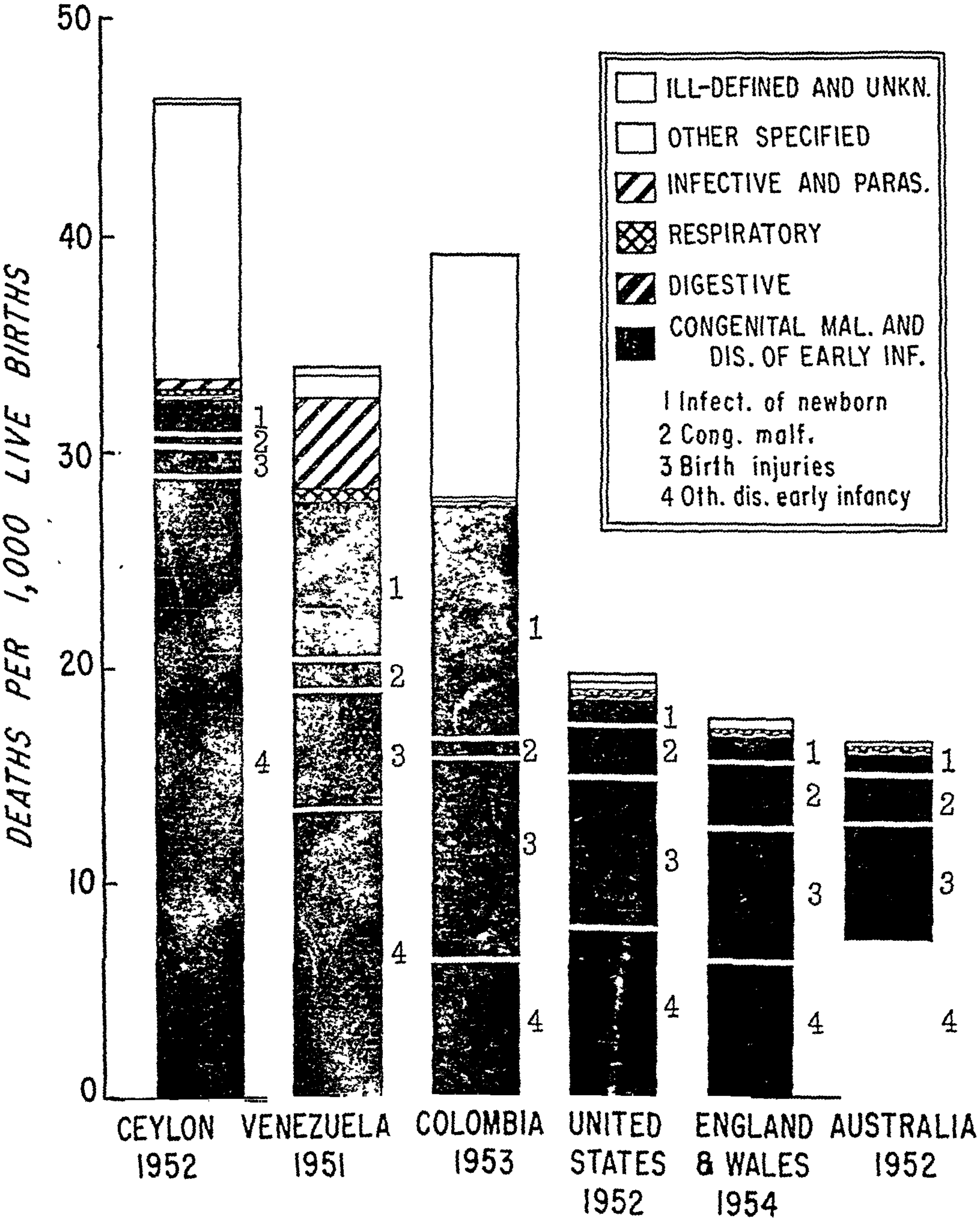


Fig. 6.—Neonatal deaths per 1,000 live births by cause for six selected countries.

Further study of the problems related to the definitions of immaturity by weight is needed, since they have implications for program planning. Only differences within the same ethnic group allow us to infer that environmental circumstances influence the distribution of birth weights. The following evidence is suggestive. Van Gelderen, Posthuma, and De Haas[6] found that the average birth weight in the Netherlands has increased by approximately 250 Gm. (0.5 lb.) in the last 20 years. Data presented at the Second Inter-African Conference on Nutrition, Fajara, Gambia, 1952, showed consistently lower birth weights of infants born of mothers in nonpaying maternity wards than in paying wards.

TABLE 2.—*Fetal and Neonatal Deaths per 1,000 Births by Cause for Birmingham, England, 1952-1954* [5]

	Total			Fetal Deaths			Neonatal Deaths		
Cause of Death	Total	Premature	Mature	Total	Premature	Mature	Total	Premature	Mature
All causes	38.8	22.7	16.1	21.8	12.0	9.7	17.0	10.7	6.3
Antenatal									
Toxemia	5.9	4.6	1.3	4.5	3.3	1.2	1.3	1.3	0.0
Separation of placenta	4.1	3.3	0.8	1.9	1.1	0.7	2.2	2.2	0.1
Other	4.0	2.3	1.7	2.4	1.3	1.1	1.6	1.0	0.6
Intranatal	7.5	2.2	5.2	4.9	1.3	3.6	2.6	1.0	1.6
Postnatal	2.3	0.8	1.5	...	...	...	2.3	0.8	1.5
Fetal abnormality	7.6	4.0	3.6	3.7	2.6	1.1	3.9	1.5	2.5
Prematurity and unknown	7.1	5.5	2.0	4.1	2.1	2.0	3.0	3.0	...

Within four racial groups in Malaya and Ceylon these differences varied from 130 to 410 Gm (0.25 to 1 lb.). For the Caucasian race, some displacement to lower birth weights was found in World War II in the Netherlands [14] and an extreme displacement to lower birth weights was found during the starvation period of the Leningrad siege in 1942.[15]

Mortality and Social Class

Finally, in a consideration of the role of the environment, there are obviously many social and economic factors determining the outcome of pregnancy, the condition of the child at birth, and his chances of survival. Utilizing the Registrar General's Decennial Supplement for England and Wales in 1951 [16] (fig. 8 and table 4), the mortality was lowest for the professional class, with a continuous increase to class 5. Furthermore, there was a difference in the increase in mortality in the three periods analyzed; from class 1 to class 5 the increase was 58% for fetal mortality, 72% for neonatal, and 278% for postneonatal mortality. The influence of social class can also be seen for various causes of infant mortality. In England and Wales in 1950, the death rate from pneumonia and gastroenteritis combined was five times as high in the unskilled as in the professional class, while the death rates from congenital malformations, birth injury, and asphyxia and atelectasis were less than twice as high in the unskilled as in the professional class.

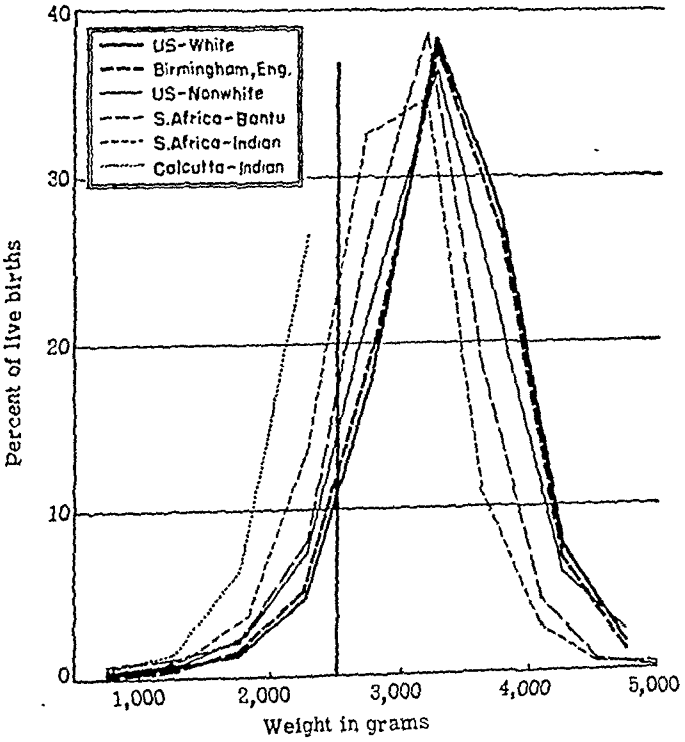


Fig. 7.—Percentage distribution of live births by weight in grams for six selected areas or groups.

Comment

In considering the challenge of fetal loss and infant mortality on a world-wide basis, the following general observations appear relevant. Sharp differences exist between technically developed and less developed areas. In the former areas, mortality has been considerably reduced in the age period 1-11 months and almost completely reduced in the next age group, 1-4 years. In contrast, much smaller declines have occurred in neonatal mortality, and it can be assumed that the declines in fetal mortality have been of the same order. The reductions in neonatal mortality have been particularly small in the early neonatal period. This results in perinatal mortality assuming an increasingly greater importance and becoming the major problem of wastage of life in technically developed areas.

TABLE 3.—*Deaths Under One Week of Premature Infants, with Rates per 100 Live Births, According to Birth Weight for Calcutta* [9] *and for White and Nonwhite Population in the United States*

	Calcutta (Jan., 1952-Feb., 1954)			United States (Jan.-March, 1950)					
				White			Nonwhite		
		Deaths Under 1 Wk.			Deaths Under 1 Wk.			Deaths Under 1 Wk.	
Weight, (Gm.)	Live Births	No.	Rate	Live Births	No.	Rate	Live Births	No.	Rate
Total	2,271	208	9.1	49,934	8,092	16.2	11,703	1,663	14.2
1,500 or less	121	81	66.9	7,268	4,866	67.0	1,741	1,029	59.1
1,501-2,000	410	74	18.0	9,206	1,782	19.4	2,182	337	15.4
2,001-2,500	1,740	53	3.1	33,460	1,444	4.3	7,780	297	3.8

For the technically less developed areas, while the perinatal mortality rate is relatively higher than in the developed areas, the mortality in the age period after one month is considerable, and there is, in addition, excessive mortality in the pre-school-age period. Here the most important fraction of wastage in child life is in the period one month to 4 years. This has great importance in program planning, since the excessive mortality in infancy and in preschool age is essentially the result of causes strongly dependent on environmental conditions, namely, gastrointestinal, respiratory, infectious, and parasitic diseases and the underlying influence of malnutrition. These causes can almost entirely be eliminated through the development of a health program that, besides supplying personal advice to the mother and the family, will aim at control of communicable diseases and improvement of basic sanitation and of nutrition; this is ultimately dependent on a broad program of socioeconomic development. This is further corroborated by the selective effect of social class on fetal, neonatal, and postneonatal mortality, with the greatest reduction in postneonatal mortality, which is more strongly influenced by the environment. Although less evident, these same causes influence late neonatal mortality. Some specific causes, such as syphilis and tetanus of the newborn infant may unduly increase the early neonatal mortality. It has been reported that in many villages in rural China tetanus neonatorum caused from 15 to 20% of the deaths of newborn infants during the first month of life.[17] Where such diseases cause many deaths, their reduction through specific attack may then produce a marked decline in early neonatal mortality. There is, furthermore, evidence that poor nutrition plays a role in increasing fetal loss and prematurity and in lowering the birth weight of the mature infant.

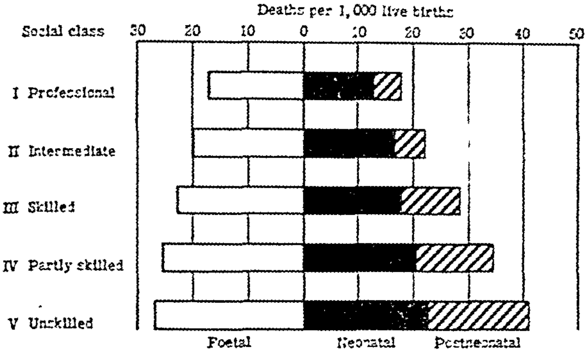


Fig. 8.—Fetal, neonatal, and postneonatal deaths per 1,000 live births by social class, England and Wales, 1950.

There seem to be three phases of action for the *solution to this problem. In less developed areas* a first point of attack is to establish basic public health services, including maternal and child health and improvement of nutrition; this will have considerable influence on survival from conception to school age. Within this program, the introduction of some specific measures may produce good results even in unfavorable rural circumstances in less developed areas. Thus, emphasis on the need for prenatal supervision to all pregnant women, including treatment of important infectious diseases and correction of severe anemia and of poor nutrition, will lower fetal loss and prematurity and increase birth weights. Provision of limited facilities for delivery of difficult cases and emergencies and education of the village midwives to prevent malpractice will save many lives during and immediately after birth. Also, attack on diarrheal disease through specific measures and improvement of weaning diets by early introduction of proteins in the feeding, supplementary to breast-feeding, will save a tremendous number of lives in many areas of the world.

The next point of attack is the one that has been met partly by most of the technically advanced countries that have had well-improved health conditions for the past 15 years. These countries embarked on a series of specific measures of attack aiming at further reduction of maternal and infant mortality. The success of national programs, such as the Emergency Maternity and Infant Care Program (EMIC) in the United States and the program for improved nutrition and care of mothers and children in the United Kingdom, launched during World War II, has been the result of efficient program planning and development, concomitant with fuller employment and increased family income.

Rapid declines led to recognition of the need for emphasis on the perinatal period and for team approach, with full integration of obstetric, pediatric and nursing skills, through the prenatal, natal, and postnatal periods which require highly specialized techniques in care. Further declines in perinatal mortality have resulted in rates below those that only a few years ago were considered irreducible. Thus, in limited groups,[3] under highly favorable circumstances, perinatal mortality has been reduced to 20 per 1,000 births, with approximately one-half in late fetal and one-half in early neonatal life. However, national mortality figures for advanced countries remain between 30 and 40 per 1,000 births, and the reduction to 20 per 1,000 will represent considerable financial and professional effort which may at present be beyond the possibilities even of some highly developed countries.

Today, increasing numbers of children with handicaps from fetal abnormality, prematurity, and birth injury can be saved. Official and private efforts for medical, educational, and social rehabilitation of handicapped children have made it possible for them to achieve their highest potentiality and to be fully integrated in their community. Yet, emphasis on prevention is justified, since the process of rehabilitation is almost invariably costly and even a slight residual handicap curtails opportunity for fullest development.

TABLE 4.—*Fetal, Neonatal, and Postneonatal Deaths per 1,000 Live Births by Social Class, England and Wales, 1950* [16]

Social Class	Fetal	Neonatal (under 4 Wk.)	Postneonatal (4 Wk.-1 Yr.)
All classes	23.1	18.5	11.3
1. Professional	17.0	12.9	5.0
2 Intermediate	20.0	16.4	6.1
3. Skilled	22.6	17.9	10.6
4 Partly skilled	25.3	20.5	14.0
5. Unskilled	26.8	22.2	18.9

Until fairly recently, congenital abnormalities were believed to be essentially the result of innate factors. But ever since maternal rubella was proved to influence the development of congenital abnormalities, this belief has been under constant attack. Today, newer knowledge points to the influence of environmental factors on the development of malformations and other handicaps. Mothers of children with cerebral palsy, epilepsy, mental subnormality, and behavior disorders have been found in a study to have had complications during pregnancy and childbirth more frequently than did mothers of normal children.[18] Since these complications also result in increased fetal loss and prematurity, a continuum of reproductive casualty with lethal and sublethal effects is suggested.

The concept of perinatal hazards, while limited to a narrow time period in terms of mortality, is considerably broadened by the recognition that they result from unfavorable circumstances in pregnancy and in early life of the mother and that their effect may be felt through a handicapped condition necessitating special care and attention throughout life.

No doubt, improved methods of care will continue to be part of a program aiming at the reduction of perinatal mortality. However, the future points to the value of a broad program of research for preventive action that might eventually break the vicious circle between the unfavorable preconceptional and prenatal circumstances and their effect on the offspring. If successful, this program, as a last and newer point of attack, should greatly influence the situation in countries with present low infant mortality rates and may also benefit the less developed areas. Present programs with emphasis on medical care have limited possibilities in these latter areas for lack of both the great financial expenditures and the highly specialized rofessional skills and facilities which they require. ut if, through future knowledge resulting from search, more easily applicable preventive measres are made available, these could become part of the broad program of development of health services. These measures may then result in more effective prevention of fetal loss and greater saving of lives in early infancy, even in economically less developed areas.

Summary

Data on fetal loss, prematurity, and infant mortality on a world basis, within the over-all picture of mortality in childhood throughout the world, point up the excessive mortality still prevailing in economically less developed areas in the age groups of 1-11 months and 1-4 years and the great reduction of mortality in those same age groups in the technically developed countries. This reduction places the major problem of mortality in childhood in these latter countries in the perinatal period.

The causes of fetal loss and neonatal mortality are interrelated, and there is a need for a definition of perinatal mortality that allows comparison of data from countries with greatly different conditions. In addition, taking account of the importance of prematurity in relation to perinatal mortality, the use of the present definition of prematurity, based on weight, creates problems when countries, areas, or groups with different birth weight distribution curves are analyzed.

For reduction of perinatal mortality, a first attack on excessive postneonatal and preschool-age mortality may be made through the development of adequate general public health and maternal and child health services. These may considerably reduce mortality in those age groups and will also, to some extent, affect neonatal and, therefore, perinatal mortality. Such programs as premature infant care and rehabilitation of handicapping conditions have achieved considerable reduction in infant mortality rates in some countries. However, an intensive program of research for the prevention of those conditions that determine the size of perinatal mortality rates appears, at present, necessary. The discovery of adequate preventive measures not only would allow further reduction of the perinatal problem in highly developed countries but might prove more generally applicable in technically less developed areas than programs of specialized care which are too costly and require too highly specialized skills and facilities to have any real effect within the low priority for program planning that can be given them at the present time.

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THE TREATMENT OF PSORIASIS AND OTHER DERMATOSES WITH TRIAMCINOLONE (ARISTOCORT)

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Sixty patients with psoriasis were treated with triamcinolone, a corticosteroid, in doses of 12 to 16 mg. daily by mouth. In 36 of the patients the response was prompt and unquestionable; within a week, the scaling and erythema diminished significantly, and within two to four weeks of continued adequate dosage the psoriasis was, in some patients, completely erased. Upon cessation of treatment or reduction of dosage, however, the lesions regularly returned. The remaining 24 patients failed to show any response. A wide variety of reversible side-effects were observed. Some were favorable, such as the stimulation of hair-growth in alopecia areata, and many were unfavorable, such as flushing, hyperhidrosis, facial hirsutism, and facial contour changes. Triamcinolone was found to be highly antiallergic, antirheumatic, and anti-inflammatory, and therefore useful in a variety of dermatitides; its use in psoriasis should probably be limited to acute extending cases not controllable by other means or to very extensive and severe chronic forms.

Psoriasis is a common chronic scaling skin disease which has long defied all attempts to determine a specific cause or treatment. It appears as a recurrent hereditary reaction pattern to a wide variety of known, as well as unknown, trauma.[1] Its course is capricious. Its severity may range from an insignificant pitting of the nails to a fatal exfoliative dermatitis. Treatment programs include an extremely large number of topical as well as systemic measures. None of these can be considered uniformly effective or in any way specific.

Accordingly, when Hollander and others [2] acquainted us with their finding that the new corticosteroid, triamcinolone (Aristocort), had a marked therapeutic effect on psoriasis, we immediately undertook an investigation of the effects of this new fluoroprednisolone compound (fig. 1). The present report details our findings over the year prior to writing in the treatment of 60 patients with psoriasis and 70 patients with assorted dermatological problems other than psoriasis. The initial patient has been treated for 10 months, and this report cannot, therefore, present an estimate of the long-term effectiveness and toxicity of triamcinolone.

Material

The present data are derived from direct personal observations on 130 consecutive patients, 60 with clinically identifiable psoriasis and 70 with inflammatory dermatoses. No attempt was made to select specific patients. All forms, types, and degrees of psoriasis were included for a more accurate estimate of the actual spectrum of action of triamcinolone. The 70 patients with inflammatory dermatoses were studied for base-line data on the

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relative corticosteroid activity of this compound. Rigid control data are lacking, since placebo therapy was not employed. However, only rapid unquestionable therapeutic effects were viewed as resulting from triamcinolone therapy. The minor, slight, or questionable benefits are ignored from the standpoint of evaluation.

The dosage of triamcinolone varied from 4 to 32 mg. orally each day. In the earliest phases of the study, triamcinolone diacetate was administered, but the majority of the observations refer to the free alcohol. No difference in response to these two forms could be perceived by us. Low, rather than high, dosage was often employed, in part because of the scarcity of the drug early in the study, the necessity of using caution in the early phases of any evaluation, and the relative insignificance of the clinical manifestations in some instances. Local treatment was usually interdicted.

In selected instances 0.5 and 1.0% triamcinolone cream and ointment were employed, with a blind paired control method of assay. In many of the patients the local effect of triamcinolone was ascertained by means of a skin test consisting of the injection into the lesion of 0.05 ml. of a sterile 1% suspension of triamcinolone in isotonic sodium chloride solution. This is the assay technique advocated by Goldman and others.[3]

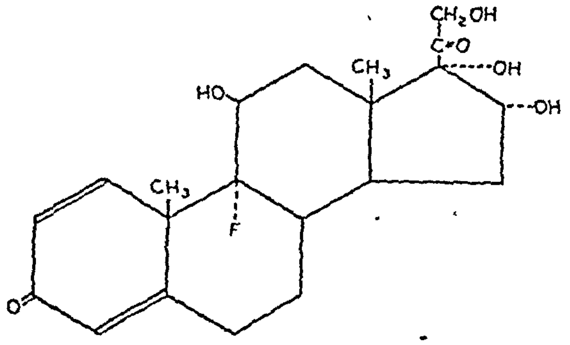

Fig. 1.—Structural formula of triamcinolone (Aristocort). It can be characterized as 9α-fluoro-16α-hydroxyΔ^1-hydrocortisone.

Results

Table 1 outlines the results obtained in the treatment of psoriasis, whereas table 2 summarizes the clinical effectiveness of triamcinolone in the treatment of some common inflammatory skin changes in which steroids have been widely recognized to be of value. It is significant to note in table 1 that triamcinolone had a prompt temporary clearing effect on as many as 60% of the patients presenting psoriasis. Furthermore, in table 2, triamcinolone is seen to be an effective anti-inflammatory glucocorticoid in a relatively small dosage.

The response of psoriasis which we have observed in the 36 of 60 patients treated was a rapid unquestionable one. Within one week the scaling and erythema had diminished significantly, and with a continued adequate dosage the psoriasis was in some patients completely erased in two to four weeks. Only residual pigmentary macular changes remained at the sites of previously scaly hyperkeratotic chronic plaques of psoriasis. Psoriasis of all areas—the palms, groin, scalp, knees, and elsewhere—fled in the responsive patient. Indeed, in long-term therapy we have seen psoriatic nails return to normal.

Triamcinolone has not been recorded by us as effective in any instance in which the morbidostatic changes were less than impressive. Quasi-improvement or delayed improvement has not been interpreted as due to the drug. The second aspect of the response which is of considerable importance is the fact that it is almost invariably reversible. Upon cessation of treatment or reduction of the dosage below the maintenance level, the psoriatic lesions have regularly returned, sometimes in more aggravated form. Within a week of withdrawal of triamcinolone, clinical evidence of psoriasis reappears or increased scaling and erythema become evident.

A full 40% of the 60 patients with psoriasis failed to show any response. What characterized this group? We could see no distinguishing feature on the basis of clinical appearance, location, or duration of lesions or the age or sex of the patient. In part, however, this nonreactive group was made up of those with recalcitrant intractable chronic psoriasis, patients who failed to respond to numerous other modalities such as ultraviolet light and tar. Most significantly, however, our studies indicated that these patients were refractory to the local effect of triamcinolone. Twenty-one patients of the group with psoriasis were skin-tested with 1% triamcinolone suspension. In each of nine patients failing to respond to triamcinolone given orally, the skin test also failed to produce a local response. In marked contrast, in each of the 12 patients showing a response to triamcinolone given orally, the skin tests showed a sharply circumscribed area of complete involution at the site of the triamcinolone skin test (fig. 2). The positive skin-test responses (fig. 3) occurred within 48 to 72 hours and persisted for weeks. Control skin tests with saline solution were without effect, although it is well known that local injection of hydrocortisone acetate may cause local involution of psoriasis.[3]

Psoriasis is far more of a reaction pattern than a disease *sui generis*. The Koebner phenomenon reflects the multiplicity of causes for psoriasis. We feel these multiple causative factors for psoriasis suggest why triamcinolone is not regularly effective. It appears that possibly triamcinolone is effective in suppressive allergic factors which trigger psoriasis in certain people. Still again seborrheic dermatitis responds so well to the compound (table 2) that one might suspect that seborrheic psoriasis may form the bulk of the examples involuting under steroid management. However, we

TABLE 1.—*Results of Triamcinolone Therapy in Treatment of Psoriasis*

Case No	Sex	Age, Yr.	Duration of Clinical Psoriasis, Yr.	Distribution	Daily Dosage (Mg.) of Triamcinolone		Observation Period, Mo	Side-effects	Clinical Result	Skin Test
					Maximum	Maintenance				
1	F	39	29	Generalized	12	..	1	None	Effective	...
2	M	52	5	Scalp, ears, nose, gluteal cleft, scrotum, penis	6	4	5	None	Effective	..
3	F	48	1	Hands, elbow, localized	6	...	1¾	Ulcer, duodenal	Effective	...
4	F	29	2	Upper and lower extremities, extending	16	...	½	None	No effect	...
5	M	45	9	Right foot, ankle	6	6	1½	None	Effective	...
6	F	60	3½	Generalized	16	12	¾	None	Effective	...
7	F	27	17	Generalized	18	...	1½	None	No effect	No effect
8	F	8	1	Generalized	8	4	2	None	No effect	...
9	M	78	1½	Left foot	6	2	3	None	No effect	...
10	M	49	15	Legs, sacrum, abdomen, nails	10	6	2	None	Effective	Effective
11	F	45	10	Generalized	16	12	1½	Cushing like changes	Effective	Effective
12	M	63	8	Generalized	8	2	2	None	Effective	...
13	F	42	7	Generalized	16	...	1	Cushing like changes	Effective	Effective
14	F	42	8 mo.	Hands	10	4	1	None	Effective	...
15	F	50	4	Elbows, knees, legs	4	1	2	None	No effect	...
16	M	41	15	Generalized	16	12	3	None	No effect	...
17	M	58	7 mo.	Scalp, face, chest, extending	8	...	6	None	Effective	..
18	F	19	6	Generalized	14	8	8	Dizziness, hirsutism	Effective	Effective
19	F	12	10	Hands, feet, extremities, extending	8	8	2	None	Effective	...
20	F	44	23	Generalized	12	...	½	None	No effect	...
21	F	51	10	Face, vulva, hands	8	4	4½	None	Effective	...
22	M	41	11	Scalp, elbows, umbilicus, penis	6	4	1	None	Effective	...
23	M	64	10	Elbows, legs, abdomen, extending	16	8	4	None	Effective	. .
24	M	73	20	Chest, abdomen, back, extremities extending	16	8	3	Weakness, leg cramps	No effect	No effect
25	M	52	2½	Scalp, ears, trunk, elbows, inguinal region, nails, extending	18	4	2	None	No effect	. .
26	F	52	8	Generalized	20	8	3	Cushing like changes	No effect	No effect
27	F	42	25	Generalized	20	12	6	None	No effect	No effect
28	F	78	7	Scalp, chest, abdomen	6	...	½	None	No effect	No effect
29	F	52	8	Hands	6	2	5	None	Effective	.
30	F	24	7	Scalp, ears, face, elbows, knees, abdomen, lumbosacral and gluteal region	10	8	1½	None	Effective	Effective
31	F	57	20	Plantar surfaces of feet	12	...	¾	None	Effective	...
32	M	51	1	Hands, heels	8	6	5	None	Effective	...
33	F	57	2½	Abdomen, scalp, back, extremities extending	12	6	7	Dizziness, Cushing-like changes	No effect	...
34	M	52	24	Thighs, sacral area, new attack	12	...	1	None	Effective	Effective
35	M	59	8	Scalp, elbows, knees, gluteal cleft	10	...	2	None	Effective	..
36	M	30	1	Fingers, nails	8	...	¾	Abdominal pain	Effective	...
37	M	39	6 mo	Scalp, face, knees	12	...	5	None	No effect	No effect
38	F	40	15	Generalized	32	8	4	None	Effective	Effective
39	F	54	5	Scalp, chest, thighs, nails, extending	8	2	2	None	Effective	Effective
40	F	58	3	Scalp, chest, inguinal region, ears, extending	12	...	¾	None	Effective	..
41	F	21	7	Generalized	12	12	7	None	Effective	Effective
42	F	24	1	Legs	12	...	1	None	No effect	.
43	M	45	3	Generalized	8	...		Gastric ulcer, pain	Effective	Effective
44	M	71	20	Hands, forearms, neck, umbilicus, inguinal region, buttocks, extending	6	...	7	Weakness	Effective	...
45	F	28	15	Generalized	16	4	1½	None	Effective	...
46	F	55	1	Ears, scalp	6	...	2	None	No effect	...
47	F	51	1	Scalp	4	...	½	None	No effect	...
48	F	59	3	Nails, elbow	4	...	2	None	No effect	...
49	F	23	3	Scalp, chest, inguinal region, gluteal region, knees, elbows, extending	12	12	1½	None	Effective	Effective
50	F	6 mo	4 mo	Scalp, eyelids, neck, abdomen, inguinal region, back	8	...	2	None	No effect	...
51	F	48	26	Knees, elbows	12	12	4	None	Effective	...
52	M	10	6	Generalized	8	...	2	None	No effect	. .
53	F	41	1	Generalized	10	6	2	None	Effective	..
54	F	43	1½	Hands, nails	8	...	2	None	Effective	No effect
55	M	57	12	Knees, hands, feet	12	...	¾	None	No effect	.
56	F	43	28	Generalized	15	. .	½	None	No effect	No effect
57	F	48	9	Scalp, arms, back, abdomen, legs, extending	16	...	1	None	No effect	No effect
58	F	48	10	Legs	8	...	½	Febrile reaction	No effect	
59	F	54	2½	Hands, feet	6	6	6	None	Effective	
60	M	53	10	Generalized	16	12	2	None	Effective	Effective

have seen classic seborrheic psoriasis fail to respond to triamcinolone. Further studies are now in progress to determine the possible prognostic value of biopsy findings. Our early impression is that an eczematoid histological cast to the psoriasis patterning is correlated with triamcinolone responsiveness.

The dosage of triamcinolone employed with success most commonly was 4 mg. orally four times a day. Dosage higher than this did not seem to lead to significantly higher improvement rates. Dosage below this may not give maximal results. Nevertheless, we have seen a number of patients respond to 8 mg. per day. The maintenance dosage is ascertained after the psoriasis is 90% cleared. Gradual tapering of the level is as critical here as with the other steroids. We commonly were unable to reduce the triamcinolone maintenance level below 8 mg. per day. At times the maintenance level would fluctuate. In a few patients use of the drug was unavoidably stopped suddenly due to an interruption in supplies. A sharp recurrence of the psoriasis was noted, and on occasion this proved to be strangely refractory to resumed triamcinolone therapy.

Table 2.—*Summary of Clinical Effects of Triamcinolone, 4 to 16 Mg. per Day, on Dermatoses Other Than Psoriasis in Fifty-one Patients**

Type of Lesion	Helped, No.	Not Helped, No.
Chronic eczematous eruptions, including atopy	14	5
Localized neurodermatitis	4	2
Contact dermatitis	6	6
Seborrheic dermatitis	9	0
Alopecia areata	4	1

* Data on nineteen other patients presenting miscellaneous eruptions are excluded because of paucity of experience in any one category.

It was with considerable disappointment that we found that 0.5 and 1.0% topical triamcinolone creams and ointments were regularly without any distinctive benefit on psoriasis. It is to be assumed that permeability factors here prevent absorption of adequate amounts, since injected triamcinolone is effective locally.

Side-effects

Side-effects of systemic triamcinolone therapy in the dosage employed by us were similar to those seen with other corticosteroids. Two patients showed a reactivation of duodenal ulcer during triamcinolone therapy. However, we found no evidence of hypertension, edema, or hyperglycemia. In five patients distinct Cushing-like changes developed—moon face, buffalo humping, and hirsutism. Hirsutism was seen as an isolated finding in an additional four patients. We feel that triamcinolone has a greater hair-growth stimulating effect than the other steroids in use. These side-effects were reversible upon stopping the therapy. An occasional patient complained of epigastric distress, pyrosis, and nausea following triamcinolone dosage. This could be corrected by the simultaneous administration of an antacid. Constipation was noted by two patients. One patient complained of palpitations, tremor, and weakness after taking each triamcinolone tablet. Another developed marked leg cramps. One patient noted a metallic taste in the mouth.

The strangest finding, seen in two patients, was the development of intense generalized flushing and hyperhidrosis about 30 to 45 minutes after a tablet of triamcinolone had been taken. In three patients, purpura developed during the triamcinolone therapy. Three patients had attacks of vertigo and fainting. In addition, one patient experienced three convulsive attacks. No direct relationship could be ascertained, but it was noted that one year prior to steroid therapy this patient had had a convulsive attack. An electrocardiogram at that time revealed no evidence of epilepsy. A number of patients showed an increase in appetite. No psychic disturbances were noted. Finally, it was gratifying to have a steroid compound which did not lead to fluid retention and edema. Indeed, several patients experienced mild diuresis and disappearance of chronic leg edema when they began triamcinolone therapy.

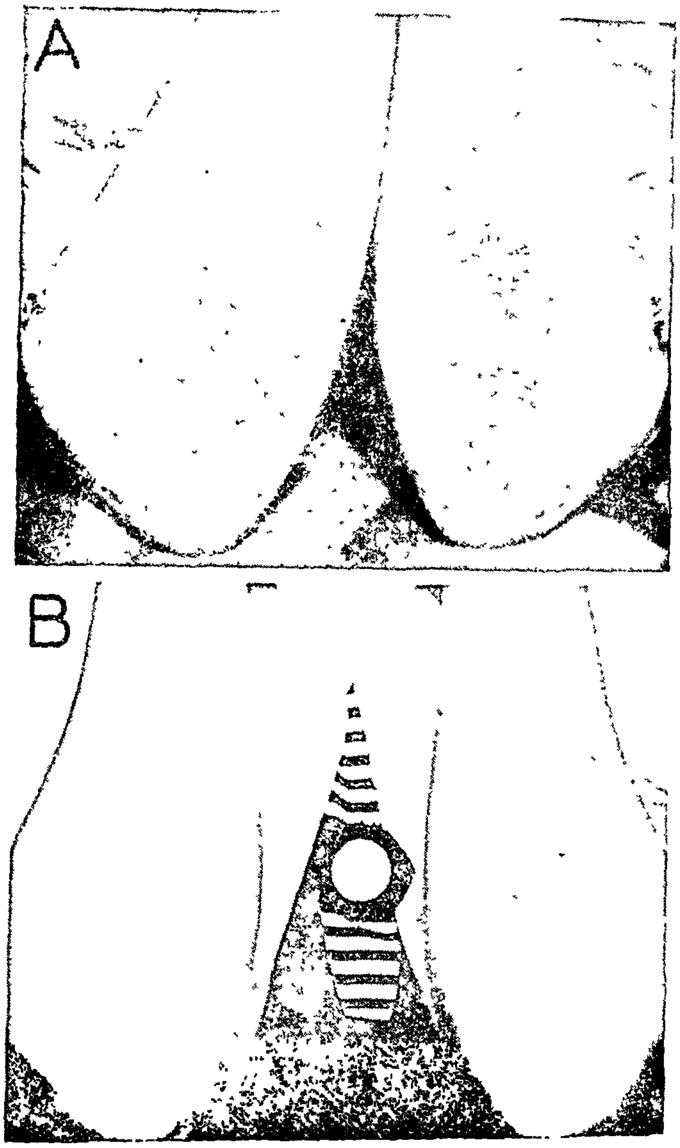

Fig. 2 (case 11).—*A*, view of psoriasis of elbows before triamcinolone treatment. These lesions had been present for many years and had failed to respond to previous local and systemic medication. *B*, view of same area after two weeks of treatment with triamcinolone in a dosage of 4 mg. three times daily. No local treatment was used.

All patients have been closely observed, and in no instance has the drug been indiscriminately prescribed. Much remains to be observed regarding the long-term effects of steroids on man.

Comment

Rein and others[4] have published their findings on the relative potency of prednisolone and triamcinolone in the treatment of skin disease. They viewed triamcinolone as significantly more effective than prednisolone. Sherwood and Cooke,[5] in studies on asthma and rhinitis, found triamcinolone twice as active as prednisone and prednisolone on an equal weight basis. Our own limited studies suggest that, although variable results may be expected in any given patient, 4 mg. of triamcinolone may be equivalent to as much as 10 mg. of prednisolone in the treatment of the dermatitides. We have seen an occasional patient in whom prednisolone was more effective than triamcinolone. In others, they appear equivalent on a weight basis.

Triamcinolone is a corticosteroid developed in a search for corticoid analogues which might be expected to have a lower incidence of serious side-effects.[6] As a fluoro-derivative of prednisolone, it has proved to be a highly effective antiallergic, antirheumatic, anti-inflammatory compound. We have asked ourselves if the action of triamcinolone on certain examples of psoriasis is a distinctive new pharmacodynamic effect or whether it reflects the well-known anti-inflammatory action of steroids. We are inclined to view the triamcinolone action as steroidal and, as such, a nondistinctive anti-inflammatory action. We have found that, although nonerythrodermic psoriasis is refractory to the usual clinical dosage of steroids, it is possible to suppress many examples by massive doses of hydrocortisone (100 mg. per day). This is in agreement with previous reports.[7] We would view use of triamcinolone as an extension of this form of therapy. Triamcinolone presumably achieves an anti-inflammatory level in the skin, which could previously be attained only by giving steroids in very large dosage. Such dosage invariably led to toxic side-effects necessitating discontinuance. It now appears that at least some of the patients with chronic severe psoriasis can be given temporary assistance without fear of severe side-effects.

Triamcinolone in common with all other antipsoriasis remedies is no cure for psoriasis. It must be recognized as purely palliative. Its use must reflect this fact. Furthermore, the physician should use it solely in an attempt to combat the severe and the generalized forms of the disease. Triamcinolone is a strong corticosteroid with influences throughout the entire body. It is not to be given for relief from a few scales on the elbows.

Triamcinolone proved to be remarkably effective in the treatment of alopecia areata. This compound seems to have a specific stimulant effect on hair growth, since hirsutism was a prominent side-effect in a number of our patients. Unfortunately, topical triamcinolone therapy proved to be without effect in the treatment of patches of alopecia areata.

In the patients in whom comparative studies could be made, it appeared that 4 mg. of triamcinolone was often equivalent to as much as 10 mg. of prednisolone in the treatment of inflammatory dermatoses. However, this was not an invariable finding, for in a few patients prednisolone proved more effective than triamcinolone when given in equal amounts. Certainly the indications for triamcinolone are the same as for the other steroids. Exfoliative dermatitis, pemphigus vulgaris, and scleroderma are other examples of disease, not shown in table 2, which responded to triamcinolone.

Summary

Triamcinolone, a new fluoroprednisolone compound, has been shown to have a significant temporary suppressive effect on psoriasis. Thirty-six of a series of 60 consecutive patients with psoriasis proved to respond rapidly and dramatically to from 12 to 16 mg. of triamcinolone daily. This group presented the distinctive finding of local involution of psoriasis at the site of injection of triamcinolone intradermally. Relapses invariably occurred when the triamcinolone therapy was withheld. Topical triamcinolone therapy was without effect in the treatment of psoriatic lesions.

In view of the rapid relapse which has invariably been noted following suspension of triamcinolone therapy for psoriasis, it seems probable that reduction of the dose to zero will offer great difficulty in many patients. On the basis of our experience to date, we have adopted an attitude of considerable conservatism in initiating such therapy, reserving it only for acute extending psoriasis not controllable by other means or for very extensive and severe chronic psoriasis. Triamcinolone also proved to have potent anti-inflammatory properties in the treatment of various other dermatitides.

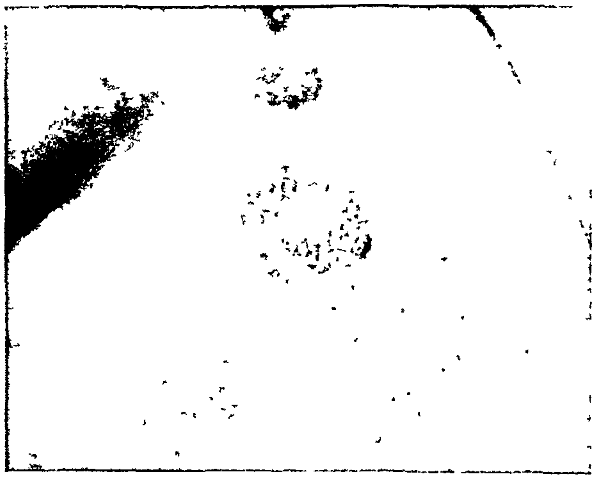

Fig. 3 (case 39).—Close-up view of psoriatic plaque showing small central clearing at exact site of intradermal injection of 1% triamcinolone suspension one week previously.

3400 Spruce St. (4) (Dr. Shelley).

The triamcinolone used in this study was supplied as Aristocort, in both tablet and topical forms, by Dr. Christopher H. Demos of the Lederle Laboratories Division, American Cyanamid Co., Pearl River, N. Y.

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STATIC AND DYNAMIC ELECTROCARDIOGRAPHIC PHENOMENA IN CORONARY ARTERY DISEASE

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The point of view is stressed that the electrocardiogram must be interpreted in terms of whether its appearance is fixed or changing. A limited number of serial electrocardiograms generally permits decision regarding the reversibility or nonreversibility of the electrocardiographic alterations. Two case histories illustrate the occasional disappearance of characteristic electrocardiographic changes of myocardial infarction. It is emphasized that the electrocardiogram as such is not generally helpful in demonstrating the extension of an acute myocardial infarct and that once a diagnosis of acute infarction has been settled on the basis of dynamic sequential changes, there is no good reason for indiscriminate repetition of the electrocardiogram.

From time to time many serious workers in electrocardiography have come to the conclusion that this soil has been so thoroughly worked over that the yield from further tillage will be negligible. Sir Thomas Lewis, for example, in about 1925, dissuaded Craib, a most brilliant and promising investigator, from further efforts in the field. Though electrocardiography is still largely empirical, attempts have been made, not entirely successfully, to change electrocardiography into a well-organized systematic and rational science. Some of the renaissance of interest in this subject has indeed come about through contact with the disciplines of biochemistry and biophysics. The important, large-scale, and continuing study of the electrocardiographic effects of various disturbances in electrolyte balance was sparked off by Winkler, and during the past few years Prinzmetal has undertaken a wholesale reexamination of the entire concept of electrical activation of the ventricular wall. The reawakened interest in electrocardiography would indicate that, as a tool of investigation, it has more than mere historical interest. The fundamental reason for this revival is a practical one, namely, the fact that the electrocardiogram, though limited in its scope, remains the most sensitive indicator of coronary artery disease, the most prevalent form of heart disease. It is estimated that there are from 15,000 to 20,000 electrocardiographs in current use in the United States. These facts justify and explain the continuing and increasing interest in the scientific and practical implications of the electrocardiogram.

The diagnosis of acute myocardial infarction may be made with reasonable accuracy on the basis of three electrocardiographic developments occurring more or less concurrently during a suspected clinical episode. These consist of sequential changes in the T wave, in the RS-T segment, and in the QRS complex. The diagnosis of old myocardial infarc-

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tion, on the other hand, is generally made on the basis of fixed changes in the QRS complex alone. The electrocardiographic representation of myocardial impairment is epitomized in the general lability of the T wave of the electrocardiogram, the transience of the RS-T interval shifts, and the permanence of the QRS complex changes. This discussion concerns certain dynamic sequences and static appearances which in some cases may have theoretical significance as well as practical clinical meaning in the diagnosis of coronary artery disease.

Three Degrees of Myocardial Impairment

It is generally accepted that the T wave, as recorded at an electrode in relation to the epicardial surface of the left ventricle, would be expected to be inverted if the left ventricular myocardium throughout its entire thickness were of uniform physiological property and the process of electrical invasion and retreat each proceeded in orderly sequence from endocardium to epicardium. It is probably because electrical retreat, or repolarization, proceeds, rather, from epicardium to endocardium that the T wave is upright in the normal heart. This has been attributed to the longer duration of the excited state in the subendocardial than in the subepicardial layers of the ventricular wall. But this T wave, and presumably the conditions responsible for it, can be altered very readily and by a host of conditions.[1] For example, experimental cooling of the epicardial aspect of the ventricle can prolong the duration of the excited state in the subepicardium so that it equals that in the subendocardium, and the T wave,. in consequence, becomes inverted. This same phenomenon can be observed in man. Drinking ice water and thus cooling the posteroinferior surface of the heart may invert the T waves in leads 2, 3, and aVF. The T-wave change is transient and disappears with removal of its cause. These thermal changes are the prototype of a mild injury to the myocardium. It needs to be emphasized that these changes are the result of intramyocardial alterations not necessarily dependent on the state of arterial perfusion of heart muscle. The experienced electrocardiographer has a whole catalogue of factors which affect the stability of the T wave. Numerous publications give voluminous testimony to this fact.

A more severe grade of injury results from the application of potassium solution to an excitable cell, tissue, or organ. Most of our information about this phenomenon has been furnished by the neurophysiologist. Potassium induces a local change in the transmembrane electrical potential, thus giving rise to a constant "current of injury." An electrode in relation to the epicardium of the left ventricle records an elevation of the RS-T segment when this injury is subepicardial in location, a depression of the RS-T segment when subendocardial. The effects of potassium represent the prototype of a more severe grade of injury than that imposed by local cooling or chilling. The RS-T segment elevation may be recorded at a precordial electrode in acute pericarditis, in acute myocarditis, in acute subepicardial, intramural, or transmural infarction. and, occasionally, for reasons unknown, as a perfectly normal variation. Nahum and Hoff[2] suggested long ago that electrical events in the subendocardium contribute little to the configuration of the electrocardiogram. This idea has recently been reformulated by Prinzmetal.[3] Perhaps this explains why in transmural infarction the RS-T segment depression which might develop in consequence of subendocardial injury is more than swamped out by the RS-T segment elevation which is attributable to the subepicardial injury.

The most severe grade of injury to the myocardium is actual death of myocardium. This process produces changes in the QRS complex which are generally irreversible. There are contradictory views regarding the origin of the QRS changes. The observations of Wilson underlie the traditional teaching of present-day electrocardiography. His observations indicate that, when an electrode which is insulated except at its tip is thrust through the ventricular wall, it records a sequence of changes as it is progressively withdrawn from endocardium to epicardium—at first, an entirely downward QS deflection at the endocardium, then a small R and deep S wave as the electrode is withdrawn into the subendocardial laminae of the ventricular wall, then equiphasic RS complexes about midway from endocardium to epicardium, then larger R and smaller S waves as it is drawn closer to the epicardium, and, finally, an entirely upright R wave at the epicardium. The translation from an endocardial QS to an epicardial R wave is predicated on the intermediation of healthy excitable myocardium. If this muscular wall is no longer excitable, the cavity QS potential is transmitted passively to the epicardium through this dead core of muscle which, though not excitable, transmits the impulse unchanged just as do other nonexcitable tissues, such as lung, bone, and liver. The cavity QS depends on outward activation of healthy ventricular myocardium elsewhere. Where the entire thickness of the ventricular wall is involved, an electrode in relation to the overlying epicardium should record a QS deflection; where a subendocardial wedge is infarcted, QR complexes should be recorded and the R wave should have a lower than original amplitude. According to Prinzmetal,[3] on the other hand, with a similar plunge electrode QS complexes are recorded in the inner three-fourths or so of the ventricular wall and the progressive build-up of more and more R wave and less and less S wave does not begin until the outer shell is reached.

Two sets of clinical observations at the Peter Bent Brigham Hospital seem to lend some support to Prinzmetal's experimental findings. The first concerns observations in pure subendocardial infarction. The following case report may be regarded as typical of my experience with this group.

The patient had a classic clinical episode, including fever, fall in blood pressure, and elevation of the white blood cell count and sedimentation rate. The RS-T segment was generally depressed. As such, this is the unusual direction of the RS-T segment shift; hence, it is referred to as an "injury against the rule." No Q wave was recorded in these leads. Postmortem examination showed a ring-like subendocardial infarct.

If the traditional view of ventricular activation is correct, one would expect QR deflections over the epicardium in subendocardial infarction. If, on the other hand, the newer concepts are sound, infarction of the inner few millimeters of the ventricular wall should have no influence on the direction of the initial ventricular complex. Since this R wave is written by the outer shell of the myocardium, inactivation of the inner shell would not be expected to affect it. Thus, one would not expect Q waves at the epicardial electrode in subendocardial infarction. In my experience with subendocardial infarction, as verified at autopsy,[4] RS, not QR, deflections were recorded in association with RS-T segment depressions.

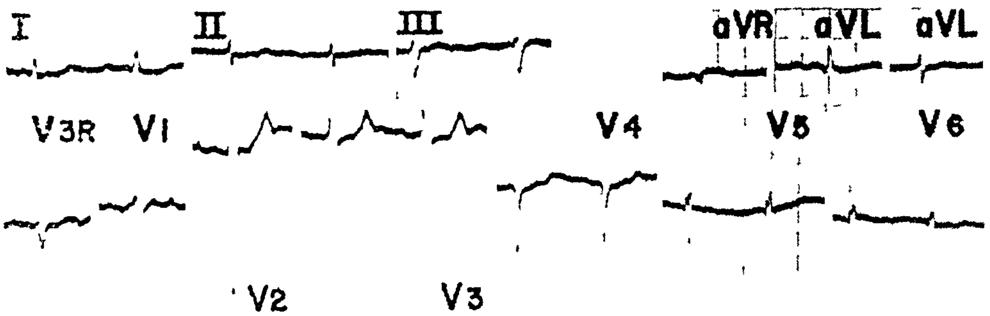

Fig. 1.—Electrocardiograms from 15-year-old boy with chronic myocarditis, proved subsequently at autopsy. Note QS complex in lead V₄. In older individual this change would almost certainly have been interpreted as indicating old anterior myocardial infarct.

The second set of experiences possibly bearing on the contention regarding the mode of activation of the ventricular wall concerns the electrocardiographic findings in constrictive pericarditis. During the past few years, experience at the Peter Bent Brigham Hospital in documented constrictive pericarditis has revealed an amazing and even disconcerting incidence of QR or QS complexes and with it the implication of actual myocardial damage. Among 26 cases, there were 4 in which an unequivocal diagnosis of old myocardial infarction was made on the basis of the electrocardiogram, 8 in which the electrocardiographic findings were in line with but not diagnostic of old myocardial infarction, and 14 in which no electrocardiographic evidence of infarction was seen. Pathological experience derived from a number of surgical spec and two postmortem examinations has sug that there is a pronounced intramyocardial sion of the epicardial eschar. Although the evic is incomplete, these findings suggest that the present experience may be reconciled with Prinzmetal's concept of free wall activation. The layer of damaged myocardium extends through the outer into the inner shell of the myocardium from which QS deflections are recorded.

It is well known, incidentally, that electrocardiographic changes quite characteristic of old myocardial infarction may be induced by a number of processes resulting in scarring of the myocardium, e. g., scleroderma, amyloid disease, hemochromatosis, and the like.[1] The electrocardiogram is unable to discriminate between the fibrosis produced as the result of vascular disease and that due to these other processes. Figure 1 shows tracings recorded from a 15-year-old boy with chronic congestive heart failure of undetermined etiology. Note the QS deflections in lead V_4. This is the sort of change which in an older individual would suggest old anterior infarct. Postmortem examination showed chronic myocarditis, with fibrosis and aneurysmal thinning of the ventricle and no coronary artery disease. Thus chronic myocarditis and chronic constrictive pericarditis must be added to the list just enumerated.

Stress Tests for Coronary Insufficiency

The diagnosis of angina pectoris is not always straightforward. Although in the great majority of patients one can establish or eliminate this diagnosis with a carefully taken clinical history, there are still a few cases with which one *must remain in some doubt.* Various stress tests, some standardized, others carried out more or less "by ear," have been proposed to help settle these doubts. Opinion is still divided as to their value. Master's group has emphasized that abnormal two-step exercise tests are not specific for coronary artery disease since other organic or functional states, such as rheumatic, luetic, or congenital heart disease or severe anemia, may be the underlying cause. On the other hand, the test may be abnormal in from 6% to 8% of normal people and also in patients with neurocirculatory asthenia or anxiety states. They further claim that, where the test is abnormal, differentiation between a true and a false-positive test may be made on clinical grounds, which makes one wonder wh in such cases the test should be done at a sson fr own experience: never do a in a whom you know full well h al he merely to atisfy him no o disease. e may we a p

The varying experience of the Hopkins group[5] would, if confirmed, cast considerable doubt on the validity of the entire Master test approach to the diagnosis of coronary insufficiency. These workers found that the electrocardiographic response to exercise was positive by Master's criteria in 22.8% of normal controls and in 50% of subjects with angina pectoris or old myocardial infarction. The experience at this hospital, not yet tabulated in detail, lies somewhere between these extremes. We have found the test to be quite helpful in certain doubtful cases. The occasion for doing this test is infrequent. We have had a very high yield of equivocal results. In the tracing recorded immediately after exercise, which is generally the most informative, the base line frequently wanders so widely that it is difficult or impossible to determine the true point of reference. Furthermore, the RS-T junction (point "j") may not break sharply but, rather, form a smooth, indeterminate slur. We have not considered the test positive unless the depressed RS-T segment moves horizontally or downward before regaining the isoelectric line. Master[6] has recently recommended the routine use of leads 2, V_3, V_4, and V_5 over the formerly used leads 1, 2, 3, and V_4 in the performance of his test.

The RS-T segment depression which is characteristic of spontaneous or induced coronary insufficiency resembles that seen in subendocardial infarction. By analogy, it is held that it is the subendocardial laminae which are vulnerable to the effects of hypoxia in coronary artery insufficiency. It is important to remember that a similar, if not identical, electrocardiographic picture may be produced by digitalis in therapeutic doses. There is some evidence that digitalis in toxic doses may actually produce myocardial necrosis and that this damage may have a predilection for the subendocardial laminae of the ventricle. There may be an enhancement phenomenon here, too, for it is quite well established that digitalis itself may induce a "false-positive" Master test, in the absence of coronary artery disease. A tracing reproduced by Yu and Soffer[7] shows diagnostic RS-T segment depressions during and after exercise after digoxin administration and no such change without digoxin. A new wrinkle is introduced into the exercise test by the Rochester workers,[8] who have utilized a three-minute treadmill test with a precordial lead. The exercising limbs do not interfere with the recording of the precordial lead, and the latter is generally much more useful than an extremity lead in the detection of coronary insufficiency anyway. With this technique these workers have found, in certain instances, diagnostic changes only in tracings taken during exercise, thus augmenting the sensitivity of an exercise test.

A study by Ramsey and Beeble[9] showed that most patients with mitral stenosis of moderate severity had positive Master tests. Many of these were in patients not receiving digitalis. An example of this is shown in figure 2, made from tracings which these workers were good enough to send me. Note that cupped depressed RS-T segments were present before exercise and that pronounced shifts were recorded after exercise.

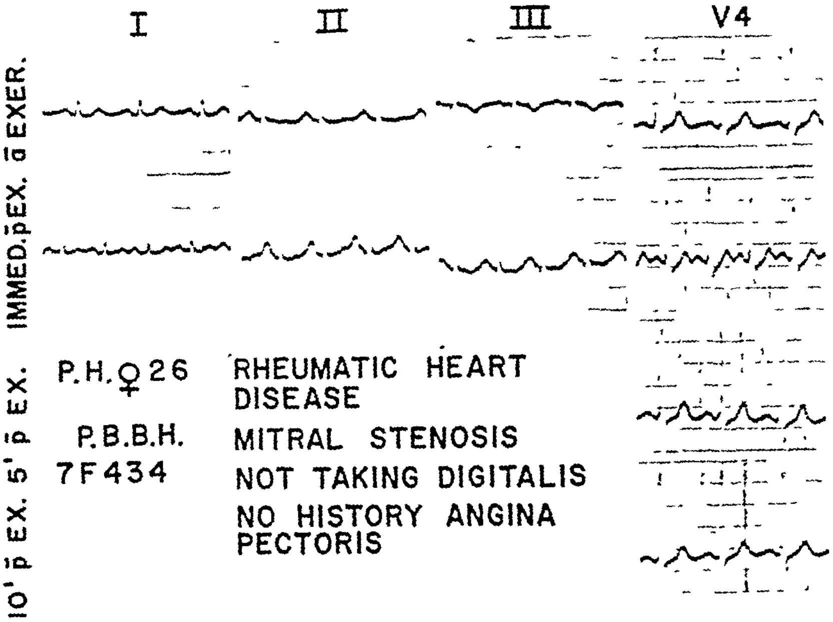

Fig. 2.—"Positive" Master test in absence of coronary artery disease. Patient was 26-year-old woman with rheumatic mitral stenosis, not taking digitalis.

The beat after a long pause may exhibit precisely the same QRS complexes as the beats preceding the pause, but its T wave may differ widely from the antecedent T waves. This would therefore correspond to what Wilson has called a "primary" T-wave change. It was first considered that this phenomenon occurs only after the pause set up by extrasystoles. Accordingly it was given the polysyllabic tongue-twister, "postextrasystolic T-wave changes." However, similar changes have also been observed in the beats after the pauses in sinus pauses, sinoauricular block, second degree auriculoventricular block, conducted or nonconducted auricular premature beats, and auricular fibrillation, as well as in ventricular premature beats. The height and direction of the T wave, of the U wave, or of both and the duration of the Q-T interval may be affected. As a general thumbnail rule, these changes should not be regarded as significant unless they are striking, compelling, and obvious at first sight. It has been our continued experience at the Brigham hospital [10] that changes of this type are usually correlated with myocardial impairment, generally myocardial ischemia. There is some degree of correlation between this postpausal T-wave change and the so-called positive Master test. In fact, we have come to look on the scrutiny of post-extrasystolic beats as a "built-in Master test." This phenomenon has been explained variously as the direct result of changes in cycle length per se, in the degree of diastolic filling and systolic emptying of the ventricles, in the volume of coronary flow, or in the contact of a distended ventricle with the chest wall.

Serial Electrocardiograms

I would like at this point to make a few derogatory remarks about the widespread habit of recording frequent and unnecessary electrocardiograms in patients with acute myocardial infarction. I have seen the most flagrant examples of this practice among interns in whom it is condoned as a necessary part of their education. But this custom is not confined within hospital walls; it is rife among practicing physicians. At $5, $10, or $15 per set of tracings, this further increases the already difficult financial burden of the patient.

When the clinical diagnosis of acute myocardial infarction is suspect and electrocardiographic support for that diagnosis is yet lacking and no alternative diagnosis has been established, one can have no quarrel with the recording of serial tracings. Sometimes it takes days or even weeks for such changes to appear. But it must be insisted that once a diagnosis of acute infarction has been settled on the basis of dynamic sequential changes there is no good reason for willy-nilly repetition of the electrocardiogram.

The most common reason given for ordering repeated electrocardiograms is to obtain evidence for extension of infarct. Yet it is only under the most unusual circumstances that the electrocardiogram, as such, gives evidence of this development. The electrocardiogram, in fact, is notoriously inaccurate in demonstrating extension. Much more often than not the clinical story of redevelopment of pain, dyspnea, shock, or sweating is much more helpful in making this inference. Many electrocardiographers, from the finding of absent R waves perhaps in leads V_1 and V_2 at the initial examination and absent R waves in leads V_1 through V_4 or V_5 at a subsequent recording, will conclude that the area of anteroseptal myocardial infarction has widened. On the other hand, one of the electrocardiographic clues to pulmonary embolism is a leftward migration of the so-called transitional zone. The latter is the precordial point or area to the right of which one type of potential, e. g., RS, and to the left of which another type of potential, e. g., QR, is recorded. Such a twist of the heart might be assumed if this transitional zone moved during a clinical episode from, for instance, position V_2 or V_3 to or beyond V_6. Moreover, RS-T segment elevations and T-wave inversions may develop over the right precordium in acute cor pulmonale, as well as in acute anteroseptal infarction. Furthermore, a shift of the transitional zone may occur in acute myocardial infarction when neither lateral extension nor acute cor pulmonale is demonstrable, presumably as the result of a slight change in the position of the heart or in the position of application of the precordial electrodes. If evidence for acute anteroseptal infarct has already been at hand, how can one say whether the change described signals extension of infarct, acute cor pulmonale, or nothing? Clearly the decision is not as easy as may at first sight appear.

Another example of this difficulty: Patients with acute posteroinferior myocardial infarction with QRS, RS-T, and T-wave changes detected initially only in leads 2, 3, and aVF, who later show the same changes also in lead V_6 or V_5 and V_6, are frequently regarded as having extended their posterior infarct laterally. Often this change occurs in the absence of clinical evidence of fresh infarction and in a day or two the changes in the left precordial leads disappear, never to reappear. One cannot escape the conclusion that these changes were present over the left precordium as a positional phenomenon, the infarctional changes rotating into and out of relation with the left lateral precordium. It would be an exaggeration, however, to say that the electrocardiogram is of no value in the detection of spread of the area of infarction.[11] If, for example, the RS-T segment elevation in leads 2, 3, and aVF has returned to or toward the isoelectric line and there now develops RS-T segment elevation and deep inversion of the T waves, as well as prominent Q or QS waves over the left precordium, the inference of lateral extension of a posterior infarct might be justified. In such a case, however, one would expect concurrent clinical changes.

Ordinarily in acute myocardial infarction one observes a characteristic progression of the RS-T and T-wave changes. At first the RS-T segment may be elevated and the T wave still upright. Then, as the degree of RS-T segment elevation becomes less pronounced, the T wave shows terminal inversion. As the RS-T segment reaches the isoelectric line, the T wave may show deeper and deeper inversion. There are many variations on this theme. One that has interested me is the occasional temporary interruption and retrogression rather than continued progression in this type of sequence. Figures 3 and 4 were each recorded in classic, uncomplicated attacks of acute myocardial infarction. In figure 3 the late inversion of the T wave, which seems to be headed to a deeper inversion, is halted temporarily, but the sequence of deeper and deeper inversion is resumed in subsequent tracings. A similar phenomenon is observed in figure 4, where the usual sequence is transiently interrupted.

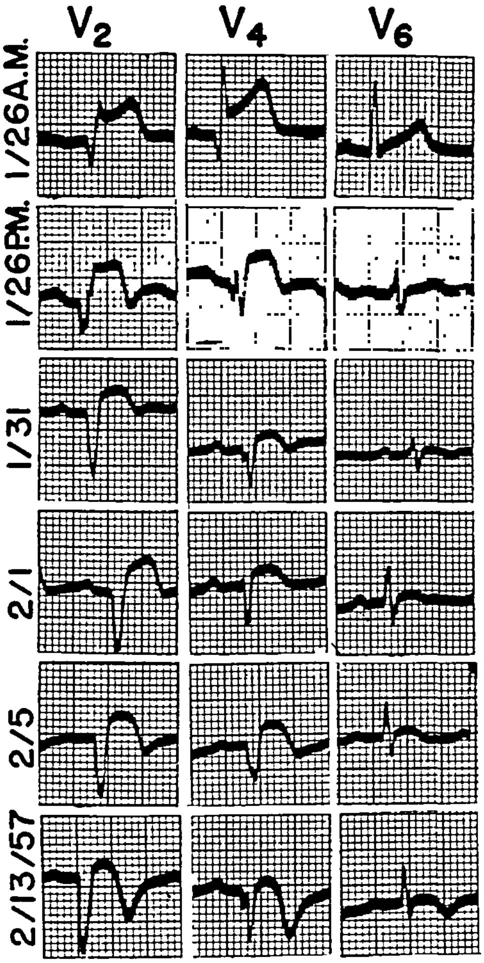

Fig. 3.—Interrupted sequence of electrocardiographic changes in acute anteroseptal infarction. Tracing of 2/1/57 shows retrogression toward earlier type of change without coincident exacerbation of symptoms; in subsequent tracings characteristic sequence is resumed.

When a series of this kind was first observed, the tendency was to attribute it to an error in the chronologic dating of the electrocardiograms, but with further experience it became clear that this was a real change. An authority on the subject of electrocardiography suggested that this phenomenon might be related to complicating pericarditis or perhaps to extension of the infarct. I have since studied the clinical charts of some 30 individuals showing such changes and could find nothing in their behavior or in the correlative laboratory data to confirm either of these possibilities. So many hearts with acute infarction show fibrin deposits on the epicardial surface anyway, and extension is such a difficult thing to establish in the face of such a continuum of pathological processes, as characterizes uncomplicated myocardial infarction, that either of these possibilities is generally extremely difficult to establish and, in the last analysis, is probably little more than a guess. It seems that this interrupted sequence is a benign electrocardiographic curiosity with little if any clinical or pathological counterpart. It was suspected that this change may be the result of electrolyte shifts, but chemical observations were too infrequent in these cases to establish this possibility. The phenomenon is perhaps a byproduct of the observation of frequent unnecessary electrocardiograms.

Persistent RS-T Segment Displacements

Ordinarily, the RS-T segment shifts that occur in acute myocardial infarction are transitory. The RS-T segment returns to the isoelectric line within a week or two. In some instances, however, these shifts persist for a longer time or even indefinitely. A case was reported by Rosenbaum, Johnston, and Alzamora[12] in which displacements of this type were present for more than two months. The patient had mediastinal neoplasm. Postmortem examination showed no coronary artery disease or myocardial infarction. It did show that the heart was invaded by neoplasm. Changes of this type have been observed much more frequently with aneurysm of the ventricle. In fact, persistent RS-T segment shift should be considered an important clue to that condition. The important practical point is that this finding is often misinterpreted as

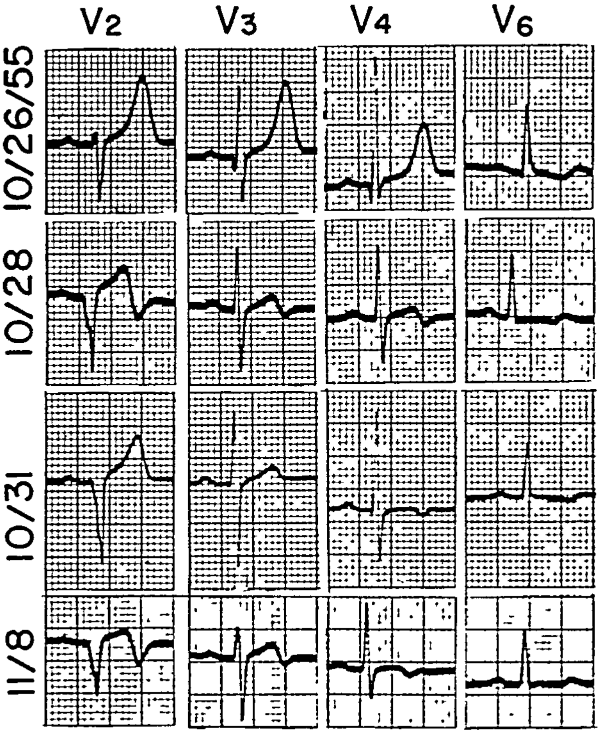

Fig. 4.—Transient electrocardiographic retrogression (similar to that in fig. 3) in acute anteroseptal infarction associated with leukocytosis and elevation of sedimentation rate. No new symptoms developed at time of interruption of sequence, final tracings show resumption of classic type of changes.

indicating an acute myocardial infarction and, in fact, is frequently the cause for repeated hospitalizations. In the absence of other laboratory or clinical data substantiating that possibility and when it is appreciated that this is a fixed rather than dynamic change the diagnosis of fresh infarction is no longer tenable.

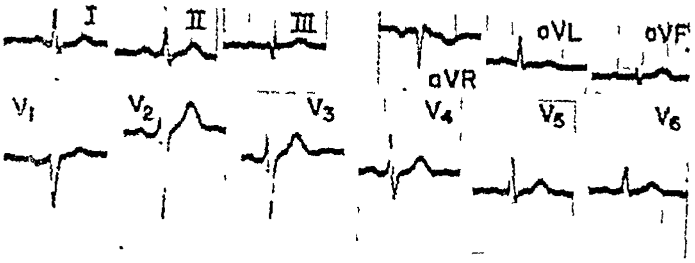

Fig. 5.—Normal electrocardiogram in patient said to have had heart attack one year previously.

Katz has considered this phenomenon a manifestation of chronic coronary insufficiency. The thesis is that, perhaps as a result of ischemic changes in the myocardium bordering on the aneurysm, electrical changes are developed repetitively with each beat. Alternatively, the changes could be explained, in part at least, by the chronic pericarditis which occurs in the overlying epicardium in many of these cases or, perhaps, by the repetitive contact of the epicardium with the chest wall producing with each beat a "current of injury." But the explanation which thus far seems best to satisfy the facts is that offered by Myers. He suggests that the changes are to be viewed as a reflection of the cavity potential inscribed at the endocardial aspect of the ventricular wall opposite the aneurysm. Since this ventricular wall is invariably hypertrophied and since the potential at the endocardial aspect of the hypertrophied ventricle is a reciprocal of the potential at its epicardial aspect, one would expect to find elevation of the RS-T segment in the cavity. The electrode "looking through the aneurysmal window" sees these changes unaltered. It must be confessed, however, that the analogy of the electrical window has been roundly criticized and that, as yet, no simple explanation is forthcoming which can explain all the electrocardiographic findings.

T Wave Changes Only

Ordinarily, changes in the QRS complex are a prerequisite to the diagnosis of myocardial infarction. There are some cases of acute infarction, however, in which changes develop only in the T waves. If these changes occur during a classic acute clinical episode and in association with other laboratory evidence of tissue breakdown, a clinical diagnosis of acute infarction is justified. The opinion that the prognosis is favorable in individuals showing such changes has recently been questioned by Cutts and co-workers.[13] If T-wave changes persist over two or three days, one must, on a priori grounds alone, suspect the possibility of actual myocardial necrosis even if there is no correlative clinical or laboratory evidence for infarction. The hypothesis would be that myocardial ischemia, long continued, must inevitably lead to necrosis. At autopsy, such hearts may show either intramural infarction or multiple punctate subendocardial necroses. Apparently the latter do not present over a large enough front to produce RS-T segment shifts. At times, T-wave inversion may be limited to the mid-precordial leads. Such a change noted during a suspect clinical episode may represent the premonitory stage of acute transmural infarction and is thus an indication for recording serial electrocardiograms.[14]

The Vanishing Infarct

Let us suppose that a patient tells you that he was treated a year ago at another city by another physician and that he was told that he had had a heart attack. Suppose also that you now find him quite unremarkable on physical examination and that the electrocardiograms which you record look like those in figure 5—a normal electrocardiogram. You might well harbor the suspicion that the previous examining physician was either a rascal or a fool. If you now contact this physician he might well send you a series of tracings recorded 15 months previously, which are classic for acute anteroseptal infarction (fig. 6). In point of fact, each set of tracings was recorded in the same patient on separate admissions at the Peter Bent Brigham Hospital on the dates indicated. The patient's story and his physician's diagnosis were, therefore, well founded.

Changes in the QRS complex are generally the most difficult to produce and the most difficult to lose, but occasionally a pathological Q wave which develops during an acute myocardial infarct will disappear after a day or two, perhaps never to reappear. The cause of this phenomenon has never been established. It has been attributed to a "knocking out" but not actual death of myocardium. Such an explanation hardly seems applicable in the present case. Changes of this type, but less pronounced in degree, have been attributed to the contraction and virtual disappearance of the myocardial scar, but it is most unusual to observe the disappearance of such widespread and convincing evidence of infarction as this. Sometimes R waves

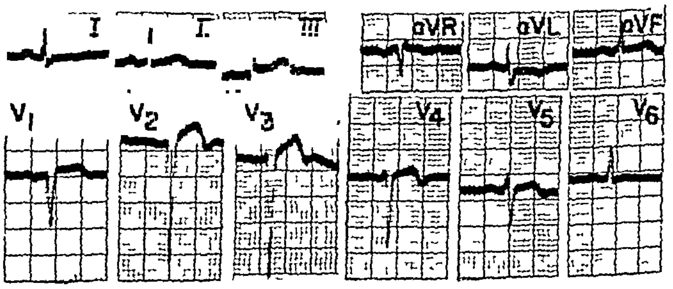

Fig. 6.—Tracings of same patient as in figure 5, recorded 15 months previously. (This was not isolated appearance but last of series of tracings showing classic evolution of acute anteroseptal myocardial infarction.)

will reappear over the right precordium in a patient with anteroseptal infarct on the supervention of a fresh posterolateral infarct. The forces activating the left posterolateral aspect of the heart are no longer present and therefore fail to antagonize the opposing forces activating the right anterolateral aspect of the heart. The latter are then able to express themselves unopposed. The fact that in the present case evidence for posterior infarction is not at hand by no means dismisses that possibility. Whatever the mechanism, the moral is clear. The experience of the vanishing infarct is not extremely rare. Whenever a patient states that he has been treated for coronary thrombosis and the electrocardiogram seems at variance with that diagnosis, an effort should always be made to study the tracings recorded at the time of the acute episode before discarding the diagnosis.

The Infarct as a Chemical Phenomenon

One of the major struts of the science of electrocardiography has been electrocardiographic-pathological correlation. For years electrocardiographers have sought vindication in the anatomic verification of their deductions from the electrocardiogram. Various explanations have been offered when such substantiation was lacking. Where, for example, myocardial infarction was diagnosed but no such anatomic lesion demonstrated, it has been at times averred that the lesion was still in its biochemical phase; the anatomic phase simply has not yet been attained. In the past, such claims have been made loosely and on a priori grounds. But support for this attitude has recently been offered by the results of the technique of histochemistry. A decrease of certain enzymes may be detected when routine staining techniques show no obvious changes. The studies of Wachstein and Meisel[15] of succinic dehydrogenase activity in clinical and experimental myocardial necrosis showed a reduction of enzymatic activity as early as two hours after the onset of symptoms and extension to fibers which showed no significant changes with routine staining techniques.

The electrocardiographic changes of acute pericarditis are generally considered to depend on changes in the subepicardial myocardium. Recent experiences in the treatment of potassium intoxication with the artificial kidney[16] raise the question of whether these changes actually result from changes in electrolyte balance, whether or not they are subsequently demonstrated to be associated with an anatomic lesion. It seems reasonable that a change which can be eliminated by dialysis should be considered a chemical change. Would this same reasoning apply to a dialyzable "current of injury"? A number of patients with acute potassium intoxication showed electrocardiographic changes closely resembling or identical with the tracings of acute myocardial infarction or pericarditis.

Before he was subjected to hemodialysis, a 40-year-old man with acute carbon tetrachloride poisoning showed changes which worried the attending staff as to the possible existence of acute anteroseptal infarct (fig. 7). This change almost completely disappeared with use of the artificial kidney but returned on the following day. He died later that day of acute pulmonary embolism. The pathologist estimated that embolism had been going on for three days or more. It is not certain that the RS-T segment shift was the electrocardiographic manifestation of acute cor pulmonale, but its elimination by dialysis was of considerable interest.

A 21-year-old man sustained severe vertebral and abdominal injuries in an automobile accident. He developed a massive intraperitoneal hemorrhage and was transfused with incompatible blood. He thereupon developed renal shutdown and potassium intoxication. On numerous occasions, in addition to the characteristic evidence of potassium intoxication, his tracings showed elevation of the RS-T segments in leads V_1 and V_2 which receded with use of the artificial kidney. This phenomenon repeated itself several times during his clinical course. He eventually recovered. (Two other patients showed similar amelioration of these shifts; at postmortem examination one of these was seen to have had definite uremic fibrinous pericarditis.)

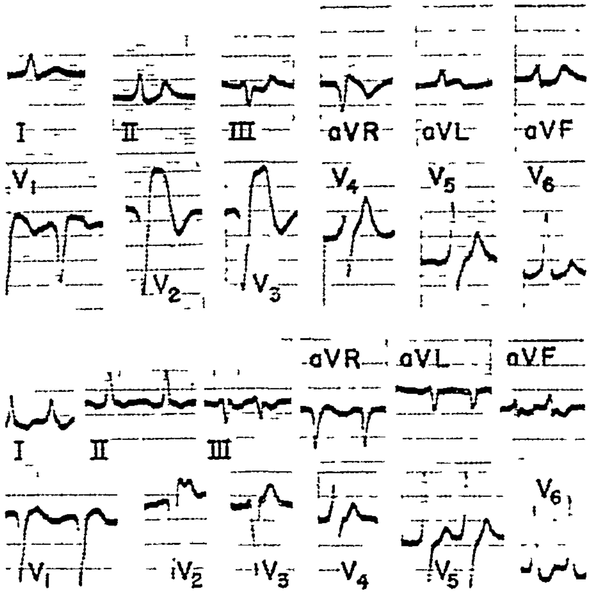

Fig. 7.—"Dialyzable current of injury": tracings recorded in 40-year-old man with acute renal shutdown. Tracings recorded before those illustrated showed classic changes of potassium intoxication and left bundle-branch block. *Above,* those recorded before use of artificial kidney show deep, broad Q waves and elevated RS-T segments over right precordium, characteristic of acute anteroseptal infarction. *Below,* after dialysis, QRS complex sharpened and shortened and RS-T elevation almost disappeared. Postmortem examination showed acute pulmonary embolism, no coronary artery disease or myocardial infarction.

When discussing the chemical aspects of myocardial infarction, one cannot help but mention the resemblance between the T waves of potassium intoxication and those of posterior myocardial infarction. In contrast to other causes of T-wave peaking, the T waves of potassium intoxication tend to be narrower, to show a greater tendency to be tall and narrow and steep and pointed, and to be associated with terminal slurring of the QRS complex.[17] However, this morphologic differentiation is difficult. Ordinarily, the clinical differentiation is not difficult because of the different setting in which each occurs, but we have now seen two or three cases in which myocardial infarction has been complicated by severe hypotension, acute renal failure, and potassium intoxication. In each of these cases potassium intoxication was the immediate cause of the fatality.

The Role of the Electrocardiographer

There are various shades of gray between black and white. Certain electrocardiographic appearances may be diagnostic of, some may be characteristic of, some suggestive of, and some merely compatible with a certain condition. Sometimes the electrocardiogram may suggest not one but a number of possibilities. It is imperative that the electrocardiographer in all honesty should list those possibilities. In doing so, he will place them in what he considers the order of their probability.

In reading x-ray films, our roentgenologist emeritus, Dr. Merrill Sosman, was in the habit of giving two readings: first, a cold reading, unbiased by the requisition form and based on examination of the films alone; second, a rereading of the films after hearing the clinical story. A similar approach has been of inestimable value in the reading of electrocardiograms. Then the clinician, whether another person altogether or the electrocardiographer functioning now as a clinician, should evaluate the electrocardiographic interpretation in relation to the clinical picture. He may find any or all of the listed possibilities to be absurd, unlikely, or impossible or he may find that they give added support to his clinical impression. It is then his duty to accept or reject them. An understanding of and sympathy with these limitations of electrocardiography is urged on the self-styled "practical" clinician or surgeon. The electrocardiographer, on the other hand, should not allow himself to be stampeded into an unequivocal statement when only an equivocal interpretation is warranted.

Summary and Conclusions

In patients with coronary artery disease it is worthwhile to note whether the electrocardiographic appearance is fixed or changing. The changes may be rapid in development, as in spontaneous or induced coronary insufficiency, slower in development, as in acute myocardial infarction, or fixed, as in ventricular aneurysm. In some cases of myocardial infarction the electrocardiogram may show changes in the T waves only; in the presence of a clearcut story and evidence of tissue breakdown, the diagnosis of infarction may be justified. The RS-T segment changes characteristic of subendocardial ischemia, if persistent over days and associated with a convincing clinical episode and correlative laboratory evidence, suggests actual subendocardial infarction. Although the electrocardiogram can furnish evidence for extension of a myocardial infarct, there is no warrant for indiscriminate repetition of the electrocardiogram once the diagnosis of acute infarction has been established. In the absence of a clinical counterpart those changes which may be observed are of dubious significance. Classic electrocardiographic signs of old myocardial infarction may be recorded in chronic constrictive pericarditis or chronic myocarditis. This results from the inability of the electrocardiogram to distinguish between fibrosis due to vascular disease and that due to other causes. In rare instances all electrocardiographic evidence of well-documented myocardial infarction may disappear.

Experience with the electrocardiogram in constrictive pericarditis and in subendocardial infarction leads some support to Prinzmetal's concept of activation of the ventricular wall.

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TRIAMCINOLONE IN TREATMENT OF RHEUMATOID ARTHRITIS

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The addition of a fluorine atom at position 9α to hydrocortisone, so-called halogenation, increases the anti-inflammatory effect over that of hydrocortisone 7 times, the antirheumatic effect 10 times, and the glycogen-depositing effect 13 times, but also increases the sodium-retaining effect to at least 50 times that of hydrocortisone. The addition of a double bond between carbon atoms 1 and 2 to form Δ 9α-fluorohydrocortisone results in about equal anti-inflammatory and antirheumatic effects but no lessening of the sodium-retaining properties. However, the addition of a hydroxy radical at position 16 to this latter compound, while decreasing considerably the antirheumatic effect (now four times that of hydrocortisone), completely neutralizes the salt-and-water-retaining properties, producing in fact what appears to be a sodium-excreting effect. Corticosteroid therapy in the management of rheumatoid arthritis should be undertaken only after serious consideration of the potentialities of the steroid used and the side-effects and other risks involved. It is most important to stress the fact that the degree of intensity of any side-effects that will lead a physician to discontinue the use of a drug, particularly a corticosteroid, is variable. Triamcinolone was found to be supressive of inflammation and rheumatic manifestations in doses roughly proportional to those of prednisone and prednisolone. The advantages of triamcinolone over previously used corticosteroids appeared to be fewer and less severe gastrointestinal symptoms, less psychic irritation, and no effect on arterial blood pressure. It was found, however, to retain many of the troublesome side-effects of the other corticosteroids.

I report here my experience with the effect of a new synthetic corticosteroid designated as 9α-fluoro-16α-hydroxy-Δ^1-hydrocortisone and its diacetate ester, triamcinolone (Aristocort). I have used it in the management of rheumatoid arthritis, osteoarthritis, and some other allied rheumatic disorders, but only my observations in the treatment of rheumatoid arthritis will be presented here.

Corticosteroid therapy in the management of rheumatoid arthritis should be undertaken only after serious consideration of the potentialities of the steroid used and the side-effects and other risks involved. It is my opinion that it should be considered in only four situations: (1) when rheumatoid arthritis is fulminating and does not promptly respond to adequate salicylate therapy; (2) when the physician is unable to maintain the patient in reasonable comfort with rest, corrective exercises, salicylates, and constitutional therapy; (3) when gold salts fail after an adequate trial; and (4) as a temporary measure just before, during, and after some orthopedic and rehabilitative procedures.

The corticosteroids are administered with too little consideration of their potentialities, particularly their untoward effects. In mild rheumatoid disorders the side-effects may well be more disturbing than the disease itself. Added to the invariable development of at least some side-effects are the possibilities of more or less dependence on the steroid, making it almost impossible to stop therapy with the drug. Also, there is the possibility of serious debilitating withdrawal symptoms and at times a periarteritis nodosa–like syndrome when therapy with the drug is finally stopped.

However, there is little doubt that the physician at times has patients with rheumatic conditions, particularly chronic rheumatoid arthritis, that may be intractable to other forms of therapy. Here a corticosteroid with minimal side-effects is the ideal sought, short of a specific cure of the basic disease itself. Since 1949, efforts have been con-

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tinuing to develop a corticosteroid with maximum anti-inflammatory and antirheumatic effects but minimum unwanted side-effects.

Chemical Structure

The addition of a fluorine atom at position 9α to hydrocortisone, so-called halogenation,[1] increases the *anti-inflammatory* effect over that of hydrocortisone 7 times,[2] the antirheumatic effect 10 times,[3] and the glycogen-depositing effect 13 times,[4] but also increases the sodium-retaining effect to at least 50 times that of hydrocortisone.[5] The addition of a double bond between carbon atoms 1 and 2 to form Δ^1 9α-fluorohydrocortisone results in about equal anti-inflammatory and antirheumatic effects but no lessening of the sodium-retaining properties. However, the addition of a hydroxy radical at position 16 to this latter compound,[6] while decreasing considerably the antirheumatic effect (now four times that of hydrocortisone), completely neutralizes the salt-and-water-retaining properties, producing in fact what appears to be a sodium-excreting effect. This new compound, triamcinolone (9α-fluoro-16α-hydroxy-Δ^1-hydrocortisone) is the one reported in this study. Sodium excretion is evident in man during the first three days of balance studies,[7] and potassium remains essentially in equilibrium. Balance studies in humans show slight but questionable loss of nitrogen, calcium, and phosphorous.[8]

Clinical Material

Since December, 1956, I have treated 105 patients with triamcinolone, all suffering from one of the following forms of arthritis or allied rheumatic disorders: rheumatoid arthritis (67), rheumatoid spondylitis (5), osteoarthritis (21), and miscellaneous rheumatic disorders (12).

At first we used the diacetate form of triamcinolone but later the free alcohol. The clinical differences appeared to be minimal and negligible. Two-milligram tablets were used, the daily dose always being given in four divided amounts, usually after meals. No dietary restrictions were advised, the subjects being allowed to use salt as they pleased. No supplemental potassium was given.

In this report only the effects of triamcinolone on rheumatoid arthritis will be dealt with in detail. The effect on osteoarthritis is a separate and distinctly different consideration in that here we are dealing with a structural degeneration, the degeneration of cartilage, the symptoms of pain probably being due to the sequential change in anatomic structure. Pain in osteoarthritis is the result of undue stress that eventually causes an inflammatory reaction of the soft tissue structures supporting the joints involved. Most observers feel that the symptoms of osteoarthritis can be handled much more effectively and with a minimum of risk by basic medical and orthopedic correction of the traumatic stresses. The corticosteroids are not needed except at times at the beginning of treatment to allay the acute discomforts of the superimposed traumatic arthritis and in patients with well-advanced osteoarthritis, where structural changes are great and the effects of these changes extremely painful and debilitating and not susceptible to medical or surgical orthopedic measures.

The subjects with rheumatoid arthritis totaled 67. Twenty-three of these were treated for at least 6 months and up to 11 months. Of the total of 67 patients with rheumatoid arthritis, 44 are still under treatment with triamcinolone, while therapy with the drug was stopped in 23 patients before six months for the following causes, some patients showing two or more of those mentioned: weakness and fatigue (6), tachycardia (5), leg cramps (5), minor gastrointestinal complaints (5), recurrence of old duodenal ulcer symptoms (1), emotional unrest (4), headache (3), hirsutism (3), persistent respiratory infection (1), glucose tolerance decrease (1), excessive weight gain (1), no improvement (1), and unrelated death (1).

It is most important to stress the fact that the degree of the intensity of any side-effects that will lead a physician to discontinue the use of a drug, particularly a corticosteroid, is variable, some ignoring any but the most marked side-effects, even going to the extent of trying to counteract the side-effects by therapy, such as insulin for patients with increased diabetes or alkalizers for patients with peptic ulcer symptoms, rather than decreasing the dose or eliminating the drug. It is my opinion that this is a dangerous procedure. In such conditions as disseminated lupus erythematosus, where the corticosteroids are lifesaving, there is justification for such a policy. I do not think it is justified in rheumatoid arthritis. In this study I have discontinued the use of corticosteroids when the side-effects were even slightly greater than minimal. This difference in attitude as to the relative importance of side-effects from corticosteroids is widespread and makes it almost impossible to compare the published incidence and degree of side-effects resulting from the various compounds so far studied.

Long-term Administration

Twenty-three of the 67 patients have received the drug for over 6 months and up to 11 months. All 23 had unquestioned rheumatoid arthritis, the average duration of the disease being over 15 years. They were well advanced in their disease, mostly in stage and class 3 and 4. Nineteen of the 23 had been on therapy with prednisone or prednisolone before starting therapy with triamcinolone, all but one for over a year, and all of these patients had experienced one or more side-effects, usually severe enough to make it desirable or obligatory that steroid therapy be changed or stopped.

The therapeutic results were good, 16 of the 23 showing a grade 2 and 6 a grade 3 response. In one patient, therapy with the drug had to be stopped after six months because of a lack of satisfactory therapeutic response from doses greater than average, even though he showed no important side-effects. How many of the good results will be maintained after 6 to 11 months is a question only the future course can answer. With previously used corticosteroids it was fairly common for initial good results to decrease or disappear even after months of satisfactory suppressive action.

The average dose of triamcinolone necessary to maintain adequate antirheumatic effect was 10 mg. a day in four divided doses, comparable to the usually stated maintenance dose of prednisone and prednisolone. Thus in our experience the suppressive effects of triamcinolone and prednisone are about equal. As a rule, therapy was started with a dose larger than this, the initial dose commonly being around 24 mg. a day.

Undesirable Side-effects

Of the total 67 patients with rheumatoid arthritis, all without exception showed unwanted side-effects of some kind. Most of these, however, were minor. The side-effects in the 23 patients who underwent long-term therapy, particularly as compared to the side-effects during previous prednisone or prednisolone therapy, can be summarized as follows: The most notable observations were that edema and high blood pressure were not observed and, when they had been present with use of prednisone and prednisolone (in 4 of 19 and 5 of 19 patients respectively), uniformly disappeared. Euphoria and psychic unrest, usual sequelae previously, were very uncommon. In five patients who, while receiving prednisone or prednisolone, were having exceedingly severe duodenal ulcer symptoms, one with bleeding, a shift to triamcinolone resulted in almost immediate cessation of peptic ulcer symptoms. Such gastrointestinal complaints as flatulence, nausea, and epigastric discomfort were noted in some, but in only one patient in 67 could these be called a peptic ulcer syndrome, and in this patient it was a recurrence of a previously proved ulcer. However, x-rays were not done routinely. The incidence of so-called silent ulcers and the question whether these patients will develop a peptic ulcer in the future, only time and x-rays can decide. No ulcer diets, antacids, or anticholinergic drugs were used in any case. The over-all impression was that gastric symptoms, while frequently present, were far less common and less severe than those with previously administered corticosteroids.

Such unwanted effects as facial rounding, hirsutism, and cutaneous purpura were noted about equally with prednisone, prednisolone, and triamcinolone. While most patients who are on therapy with other corticosteroids gain weight, most of the patients taking triamcinolone lost weight, probably due to water loss and not to protein loss and muscle wasting, as the weight loss was usually confined to the first few weeks of the medication only. In view of the reported excessive weight loss observed by some investigators after administration of triamcinolone, I was careful to note this point. In no case was the weight loss as much as 10% of the original weight. Some of the excessive weight loss observed by others may have been in cases where the patient had been receiving other hormones and had excessive initial water retention. Also the well-recognized appetite-curbing effect of triamcinolone is undoubtedly a factor. No new diabetes developed, and in the over-all series the condition of patients who already had diabetes was not adversely affected.

One side-effect that appeared to be more frequent with triamcinolone than with other corticosteroids was leg and foot cramps, especially at night, often requiring the patient to get up and walk about. The over-all incidence in the 105 cases was about 16%. These leg cramps could not be correlated with such abnormal findings as changes in the oscillometric readings or in calcium, sodium, potassium, and other blood studies. At times, these cramps were severe enough to induce me or the patient to discontinue therapy with the drug; but if the administration was continued this particular side-effect often disappeared.

Further experience with triamcinolone over a longer time than 6 to 11 months will undoubtedly reveal other untoward effects. No observations were possible as to the presence or absence of osteoporosis sequential to the use of this drug. To date, however, this corticosteroid stands out as advantageous in four important respects: 1. There is a uniform absence of edema, probably due to its lack of salt-retaining properties. 2. Gastric irritation and peptic ulcer symptoms are less frequent. 3. There is lessened psychic irritation. 4. There is a lack of effect on the arterial blood pressure. These are the four side-effects that plagued patients most severely with previously used corticosteroids. In other respects the incidence of side-effects is similar, although their development seems to take longer on average anti-inflammatory doses. To date triamcinolone is the safest effective corticosteroid I have used.

Summary

A new synthetic steroid, 9α-fluoro-16α-hydroxy-Δ^1-hydrocortisone, and its diacetate, triamcinolone (Aristocort), used in the treatment of rheumatoid arthritis, appears to have four important advantages over other steroids in almost all cases: (1) lack of the production of edema; (2) less gastrointestinal symptoms, particularly the peptic ulcer syndrome; (3) less psychic irritation; and (4) no effect on arterial blood pressure.

Triamcinolone was found to be suppressive of inflammation and rheumatic manifestations in doses roughly proportional to those of prednisone and prednisolone. This effect was established more slowly with triamcinolone than with the other corticosteroids, but at the same time unwanted side-effects were slower in asserting themselves. Triamcinolone, however, was found to retain many of the disturbing side-effects of the other corticosteroids, particularly its masculinizing effects, facial rounding, cutaneous purpura or ecchymosis, and acne. Increased sweating and leg cramps were prominent.

580 Park Ave. (21).

The triamcinolone used in this study was supplied as Aristocort *by Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.*

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CLINICAL NOTES

CARDIAC ACTIVITY IN AN APNEIC FIVE HUNDRED EIGHTY GRAM HUMAN FETUS

MAINTAINED FOR TWENTY-ONE HOURS AT TEMPERATURES BETWEEN 22 C AND 0.1 C

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Nine years ago, the rationale for the use of hypothermia in asphyxial conditions was discussed and preliminary data were presented which showed that cooled animals tolerate longer exposures to asphyxia than do animals at normal body temperatures.[1] Subsequently, these results were confirmed and extended by experiments on several hundred neonatal and adult guinea pigs.[2] Even more striking benefits in asphyxia have been reported for hypothermia in the case of neonatal rabbits and puppies, which are less mature at birth than the guinea pig.[2b] In all species investigated, the newborn member is more tolerant of hypothermia than the adult of the same species. In addition, tolerance is greater in those species which are less mature at birth than in those which are more mature. Accordingly, it has been suggested that, in all probability, the full-term human infant can tolerate lower temperatures than the adult and that the premature infant is still more resistant to cold.[2]

Recently an opportunity was presented for studying the effects of hypothermia on the cardiac activity of a 580 Gm. (1.25 lb.) female fetus on which a craniotomy had been performed during a legal abortion. As may be seen from the account which follows, the heart of the premature fetus not only can tolerate cardiac standstill of one hour's duration at 0.1 C but, even when its oxygen supply is severely limited, actually recuperates during such periods of inactivity.

Procedure

The baby was placed in isotonic glucose solution at 2 C immediately after delivery. It arrived at the laboratory, 35 minutes later, with a body temperature of 25 C and was totally immersed in fresh

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glucose solution at 2 C. Heparinized type O blood, saturated with 95% oxygen plus 5% carbon dioxide, was delivered to the fetus at intervals through a catheter inserted into the umbilical vein. Since only a small amount of this type of blood was available and difficulties with perfusion were encountered, only 300 ml. of the blood was used during the entire period of observation. No attempts were made either to close the craniotomy incision or to staunch the flow of blood which seeped from the wound. The chief function of the perfusion blood was to replace that lost. However, at higher temperatures deterioration of the electrocardiogram (ECG) was noted when perfusion was stopped for any length of time. Since the incision was over the area of the respiratory centers, no attempts were made to induce respiratory movements.

A thermistor was inserted 4 cm. into the colon. Electrocardiographic leads from a two-channel direct-writing electrocardiograph were attached to the appendages. Throughout the entire study, the gain was kept constant at 20 mm. per millivolt and the rate of movement of the paper at 25 mm. per second. Generally, the electrocardiographic records were made at temperature intervals of 1 C during each of the five periods of cooling and rewarming.

Reduction of body temperature during the first three periods of cooling was produced by placing the basin of isotonic glucose solution containing the fetus in a larger container of melting ice. The lower temperatures during the fourth and fifth cooling periods were achieved by packing the fetus in snow after the temperature of 4 C was reached.

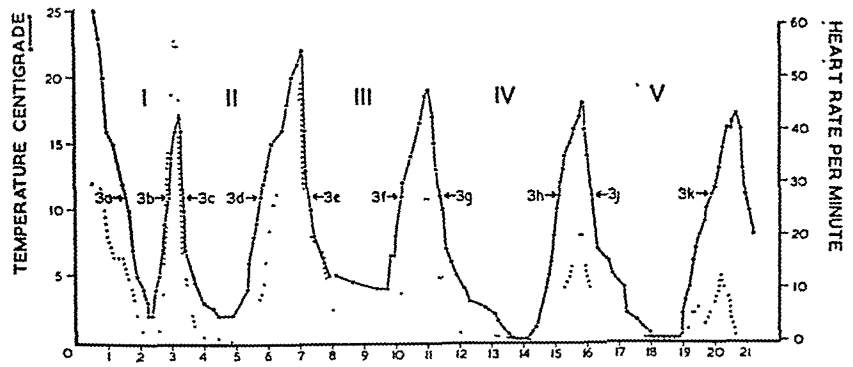

Fig. 1–Temperature and heart rate of 580-Gm. fetus during period of observation.

Observations

Temperature.–On figure 1 is graphed temperature and heart rate during the entire period of observation. From this it is seen that the temperature of the fetus reached 2 C the first and second time it was cooled. The first time it was kept at this temperature for one minute and the second time for 41 minutes. The lowest temperature during the third cooling period was 4 C. During the last two cooling periods temperatures of 0.1 C were achieved. In the fifth period the fetus was kept at this temperature for an hour before rewarming was begun.

In table 1 is a comparison of the lengths of exposure to deep hypothermia during the five cooling periods. On this is recorded the fact that the temperature of the fetus was below 15 C for over 17 hours (1,037 minutes), below 10 C for over 13½ hours (817 minutes), below 5 C for 9½ hours (576 minutes), below 2 C for 4 hours (244 minutes), and below 1 C for almost 2½ hours (148 minutes). The shortest single exposures were in the first cooling period; the longest were in the fourth or fifth periods. If deep hypothermia is a "stressful condition," the last cooling period, with 109 minutes below 2 C and 83 minutes below 1 C, should have produced the greatest challenge to the heart. Actually, as will be seen from sample electrocardiograms, heart action was visibly improved by each period of deep hypothermia.

Table 1.–*Length of Exposure to Deep Hypothermia*

Temperature	Cooling Periods, Minutes 1st	2nd	3rd	4th	5th	Total Minutes
Below 15 C	114	117	224	291	291	1,037
Below 10 C.	72	143	173	216	213	817
Below 5 C	34	106	108	174	154	576
Below 2 C	1	41	0	93	109	244
Below 1 C	0	0	0	65	83	148

The first rewarming period was arbitrarily terminated at 17 C body temperature. The length of the subsequent rewarming periods was determined by the appearance of the electrocardiogram, and it will be noted that the maximum temperature which the heart could tolerate fell with increasing time. The final stoppage of the heart is attributed to the failure to start the sixth cooling period at 15 C before irreversible changes had developed.

Heart Rate.–Since at very low temperatures there is heart block with complete dissociation of atrial and ventricular beats, the rates of the QRS complexes were plotted as "heart rate" on the graph (fig. 1, dotted line). In addition, there were irregularities in rate and conduction which will be considered later. The most remarkable aspect of observations on heart rate is that contractions were registered at temperatures down to and including 0.1 C. Although at this temperature contractions did not continue indefinitely, several beats were recorded. These were separated by intervals of as long as eight minutes before complete standstill occurred. The method for detecting such widely spaced contractions was not developed until the fourth cooling period. In the last two cooling periods, as the rate approached two beats per minute, the gradually increasing intervals between contractions were timed on a stop watch. This permitted predictions of the time of appearance of future contractions and also the recognition of ECG records in which all phases were so slowed as to be of questionable significance when seen out of context. At the lowest temperatures, QRS intervals of greater than five seconds and maximal deflections of only 0.2 mv. were encountered.

On the graph (fig. 1), it can be seen that, in general, the rate of contraction at a given temperature decreased with time. A further analysis of heart rates is made possible by comparing the rates during cooling and rewarming at temperatures of 16 C, 14 C, 12 C, 11 C, and 10 C (table 2). This shows that after the first cooling period there was an increase in rate which, up through 14 C, was more than twofold. The maximum rate during this first rewarming (and, indeed, during the entire period of observation) was 56 beats per minute at 15 C. By 16 C the rate had started to fall, and at 17 C the second period of cooling was started. Perfusion difficulties encountered during the second cooling period were reflected in the sudden drop in rate to 29 beats per minute at 16 C. Although during subsequent rewarming periods the electrocardiograms showed a great measure of recovery, the rate did not again reach as satisfactory figures as were recorded during the first rewarming period, except at very low temperatures. It may be noted that in the third, fourth, and fifth periods (but not in the second) the rates were greater at each temperature during cooling than they had been a short time earlier during rewarming (compare columns 4 and 5, 6 and 7, and 8 and 9). No suggestions are offered as to the significance of this phenomenon.

TABLE 2.—*Effects of Cooling and Rewarming on Heart Rate, Beats per Minute*

	1st Period		2nd Period		3rd Period		4th Period		5th Period	
Temperature	Cooling	Warming	Cooling	Warming	Cooling	Warming	Cooling	Warming	Cooling	Warming
16 C	40	51	29	35	44	20	22	16	20	8
14 C	20	45	21	21	41	16	18	10	12	12
12 C	16	30	24	12	32	10	14	8	10	8
11 C	15	36	20	12	...	4	12	6	9	5
10 C	12	30	20	8	24	...	12	2	8	3

Electrocardiogram.—Because the exposures to hypothermia were superimposed on varying degrees of hypoxia, hypercapnia, depletion of energy stores, and increase in concentration of waste metabolites, there are inherent difficulties in interpreting the many changes observed in the ECG. A more detailed analysis of the electrocardiographic record will be presented elsewhere. However, a few samples are shown here in order to illustrate in general the influence of deep hypothermia on cardiac activity. In figure 2 is a comparison of the electrocardiographic records taken immediately after the arrival of the fetus at the laboratory and 66 minutes later after partial rewarming from 2 C. Figure 2*a*, *b*, *c*, *d*, *e*, and *f* are records from six different leads at the start of the first cooling period with the fetus at 25 C. Figure 2*g* and *h* are records of leads 1 and aVL which were taken during the first rewarming period with the fetus at 11 C. These two are directly comparable to figure 2*a* and *e*, since the gain was kept at 1 mv.=20 mm. and the movement of the paper was maintained at the rate of 25 mm. per second throughout the entire period of observation.

An increase in the time required for each stage of the cardiac cycle is to be seen between the records at 25 C and 11 C. However, the most significant difference between the records is in the amplitude of the R wave. The potential change recorded in lead 1 was 0.12 mv. at 25 C, whereas at 11 C it was 1 mv., an eightfold increase. An increase of the same order of magnitude is seen in the records from the aVL lead also (fig. 2*e* and *h*). Decreases in amplitude, as well as slowing of the rate, have been observed in premature infants with more than optimal temperatures and with cyanosis. At lower temperatures, with an improvement in general condition, both the amplitude and the rate increase.[3] For this and other reasons, the amplitude is considered to be a good index of general condition of the heart.

In figure 3 are illustrated sample electrocardiographic records at 11 C which were made before and after each of the five periods of maximal cooling. In the upper row (fig. 3*a*, *c*, *e*, *g*, and *j*) are records taken during cooling after the fetus had been at higher temperatures. The records in the lower row (fig. 3*b*, *d*, *f*, *h*, and *k*) were taken during rewarming after exposures to much lower temperatures. Both rows show the atrioventricular dissociation and inverted P waves which are characteristic of hearts at very low temperatures.

The first record was made before the first exposure to 2 C (compare fig. 1, 3*a*). On it, the QRS complex is both low and broad (fig. 3*a*). The time occupied by the QRS complex which is commonly called "ventricular activation time" has been shown to be the time required for depolarization of the myocardium.[4] Therefore, a broad QRS complex indicates slow depolarization and a narrow one, rapid depolarization. As mentioned above, low potentials appear to be associated with poor condition of the heart muscle and high potentials with good condition.

Difficulties were encountered with perfusion during the second cooling period These were reflected in the height of the waves (fig 3*c* and *d*) Nevertheless, the rate of ventricular depolarization, as indicated by the breadth of the QRS complex, was more rapid than it had been before the first cooling period, 1 hour and 52 minutes earlier (compare fig. 3*a*). Depolarization time 3 hours and 22 minutes after birth was 0.06 seconds (fig 3*c*) From this it increased until, 11 hours and 37 minutes after birth, it was 0.8 seconds (fig 3*g*). A considerable degree of recovery was noted after the first exposure to 0.1 C, and 16 hours and 23 minutes after birth depolarization time was reduced to 0.36 seconds (*fig. 3j*).

In contrast to the records of the upper row, those of the lower row were made as the fetus was rewarming after a period at greatly reduced temperature. Important differences are seen when the records in the lower row are compared with those directly above. The QRS complexes of the lower row are taller and narrower than are those of their counterparts above. This is most noteworthy at figure 3*b* and least obvious at 3*d*. At figure 3*d*, as well as at 3*c*, blood was not flowing through the perfusion cannula at the time the record was being taken.

The recovery of the heart illustrated at figure 3*d* was the most remarkable of the series and was typical of the entire course of the first rewarming period. Until the temperature of 2 C was reached, the tracings during the cooling phase of the first period in no way foreshadowed the great increase in rate and amplitude which characterized all temperatures through 15 C during the first rewarming. At 2 C a slight elevation in potential over that in earlier records was noted. This increased steadily, until at 11 C it reached a maximum of 1 mv. At higher temperatures it diminished somewhat. The increase in heart rate which accompanied the increase in temperature likewise was more marked during the first rewarming period than in any subsequent one. As noted earlier, the maximum heart rate was not reached until the temperature was 16 C.

At no time during the 21 hours was there a clearly recognizable wave of Osborn, which was first seen in hypothermic dogs [5] and has been subsequently described for hypothermic adults, including man. Notching of the R wave, which has been emphasized by Nardone [6] as a concomitant

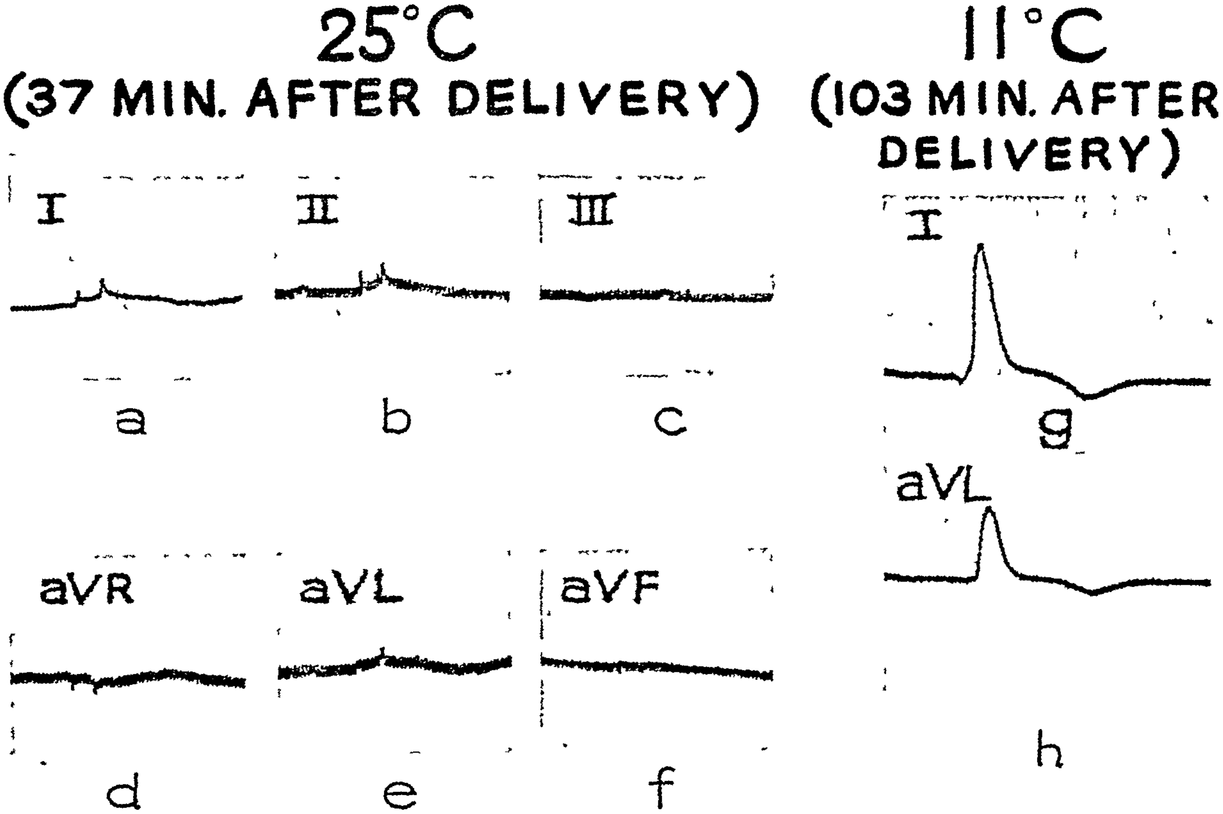

Fig 2—Comparison of electrocardiographic tracings at 25 C and 11 C Rate. 1 mm =0 04 seconds, gain: 1 mv.=20 mm.

of low temperature, is seen in figure 3*e* and particularly in 3*j*. As may be seen by comparing figure 3*e* with 3*f* and 3*j* with 3*k*, it is a reversible change.

Increasing width of the QRS complex with the passage of time is to be seen in both the upper and lower rows of records. This slowing of depolarization was not a completely irreversible one, however. Between figure 3g and 3*h* the time for the QRS complex was reduced from 0.7 seconds to 0.4 seconds after an exposure to 0.1 C. Although slowing of the QRS complex accompanied the reduction in heart rate which was observed at each temperature with the passage of time, its exact significance is problematical. The possible significance of this and other aspects of the ECG will be considered later.

Comment

This 580-Gm. fetus appears to have established several records for survival. There have been no published records of maintenance of heartbeat for more than 12 hours in apneic infants even with perfusion.[7] In addition, there are apparently no previous reports of recovery of heart action in adults, infants, or human fetuses from temperatures below 16 C. Laufman has reported one case of an adult whose temperature was 18 C 90 minutes after admission.[8] Extrapolation of the *temperature recovery* curve indicates that the patient's temperature was 16 C on admission. Dammann and Muller[9] have reported cooling a newborn infant to 11 C and obtaining recovery of heart action at about 20 C with the aid of massage. However, as the temperature rose above 26 C, the child became progressively worse, and recovery was not permanent. The heart of the fetus reported on here not only continued to contract at temperatures down to 0.1 C but, after two periods of asystole at that temperature, recommenced spontaneously on being rewarmed.

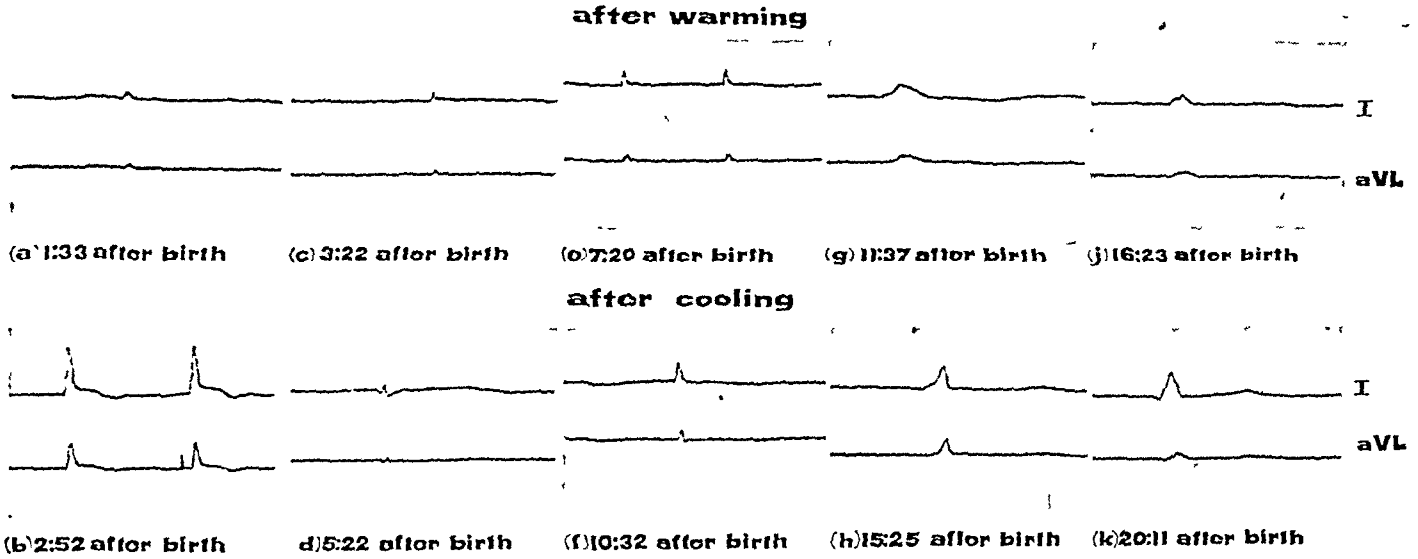

Fig. 3.—Electrocardiographic tracings at 11 C. Rate: 1 mm.=0.04 seconds; gain: 1 mv.=20 mm. (32% of original size).

Length of Apneic Survival.—The studies of Enhörning and Westin provide a standard of comparison for the effectiveness of deep hypothermia in premature infants. In fetuses maintained at 37 C without perfusion, heartbeats have been recorded for a maximum of 93 minutes. At this temperature, perfusion with oxygenated blood increases cardiac survival only slightly. At 25 C heartbeat may continue for three or four hours without perfusion. Successful perfusion at this temperature increases survival time by a factor of three or four.[7]

In the case reported here, in spite of intermittent and largely ineffectual perfusion, contractions were maintained for a much longer period. In addition, when the autopsy was performed 23 hours after delivery, exposure of the heart to air was followed by a number of contractions of the ventricules before cardiac activity ceased altogether. During the two-hour interval between termination of the experiment and autopsy, the fetus had been exposed to a sixth period of deep hypothermia, since it had been left in the solution at 2 C.

Although there appear to have been no reports of measurements of oxygen uptake of fetal hearts at 37 C, if one may assume that their energy requirements per contraction are of the same order of magnitude as those of adults, an estimation may be made of the effectiveness of 300 ml. of oxygenated blood. At 37 C the adult heart uses about 0.097 ml. of oxygen per gram per minute or 5.8 ml. per hour.[10] Since the heart of a 580-Gm. fetus weighs 5 Gm. and beats at twice the rate of the adult heart, this places its normal hourly requirements at 58 ml. of oxygen. At saturation 300 ml. of adult blood contains 60 ml. of oxygen. However, before reaching the fetal heart a portion of the blood entering the abdomen in the umbilical vein passes through the large left lobe of the liver.

Under hypoxia, this might be expected to take an appreciable toll of oxygen from the blood. In addition, only about 5% of the blood passing through the heart reaches the myocardium via the coronary system.[11] On the other hand, it must be borne in mind that, because of its thin walls, the fetal heart is less dependent on coronary circulation than the adult, because a larger fraction of its needs can be supplied by diffusion from the lumen. Equating these various factors, it appears likely that 60 ml. of oxygen in the umbilical vein could not have supplied the normal requirements of the heart at 37 C for more than approximately 15 to 30 minutes.

That total failure of the heart was so long postponed is attributed chiefly to the extremely low metabolic requirements during the 13½ hours that it was below 10 C, and particularly in the 9½ hours it was below 5 C. Fitzgerald[11] has reported a sharp fall in oxygen consumption of newborn mice below 10 C and particularly from 4 C downward. At 2 C they utilized only one-sixteenth the oxygen needed at 10 C. That a similar condition obtains in the premature human infant is suggested by the observation that the blood in the cutaneous vessels became fiery red during the periods when the fetus was packed in snow (at temperatures below 4 C). This indicated that the metabolism of the tissues was so low that sufficient oxygen diffused from the air to supply their needs and saturate the blood also.

Possible Role of Carbon Dioxide.—Although no measurements of blood oxygen or carbon dioxide were made, the presence of varying degrees of cyanosis at all times except during the two periods below 2 C is evidence of hypoxia and, associated with it, of hypercapnia. This may have contributed to the long survival of the heart of the fetus. A number of investigators have shown that it is possible to revive high percentages of mice, rats, hamsters, dogs, and monkeys from temperatures near 0 C by exposing them during cooling to hypercapnia.[12] Although hypoxia is not absolutely essential,[12b] for mice, at least, a combination of the two produces higher percentages of complete recoveries than when carbon dioxide alone is used.[13]

Carbon dioxide has several physiological effects which are beneficial in hypothermia. It reduces oxygen uptake and heat production, thereby aiding in cooling. It suppresses shivering, which elevates the oxygen requirements as much as 400%. Of even greater possible value in deep hypothermia is its well-known effect as a vasodilator, particularly of the cerebral arteries. Severe vasoconstriction is a well-documented accompaniment of deep hypothermia and may well be responsible for the damage which has been noted, from both behavior changes and histological preparations, in animals kept hypothermic for long periods.[2b]

It is possible likewise that the heart of the fetus might have developed asystole earlier if there had been no periods of rewarming or if the temperature of 0.1 C had been maintained for more than one hour. Animal experiments have disclosed a critical period between one and two hours at this temperature. In the mouse, arterial vasoconstriction* takes place during this period even though the cooling is accompanied by hypercapnia.[14]

General Implications.—The primary effect of hypothermia on cells is a reduction in the rate of chemical activity which becomes more pronounced with each degree that the temperature is lowered. This makes temperatures between 10 C and 0 C especially attractive for those interested in protecting vital organs from oxygen lack. There is no theoretical reason why temperatures down to zero should not be tolerated.

In the case of the adult, secondary effects induced by hypothermia constitute serious limitations to its use. The most serious of these result from reactions of the vascular system to cooling. Ventricular fibrillation and arterial vasospasm are two of the worst of these.

As indicated by studies on fetuses of other mammals, these secondary effects apparently do not constitute as serious a problem in the case of the newborn infant. The fetal ventricle exhibits little tendency to fibrillate; although the lowest limits from which recoveries have been reported vary, they are regularly lower for the newborn infant than for the adult of the same species.[2b]

The asphyxiated fetus would appear to be an ideal subject for treatment with hypothermia. On the one hand, mild asphyxiation increases the tolerance of cooling, and, on the other, the reduced metabolism at low temperatures protects the cells of vital organs from death caused by severe asphyxia. There appears to be no rational basis for the use of heat as part of the treatment of asphyxia. Indeed, animal experiments have shown that with no other treatment than reduction of body temperature there is 100% spontaneous recovery from exposures to asphyxia which are 100% lethal for warmer littermates.[2a]

The results of the present study suggest that the 580-Gm. human fetus more nearly resembles the newborn mouse or rat than the newborn guinea pig in its ability to tolerate deep hypothermia. About half of the guinea pigs die at 10 to 12 C,[2a] whereas newborn rats recover spontaneously from 1 C.[15]

The fact that heart action continued at temperatures below 1 C does not in itself constitute an indication for the use of hypothermia. However, the improvement in heart action after the periods of lowest temperature is evidence of its benefits. This fact strengthens the argument that, when given an adequate test, hypothermia will prove to be able to protect both the life and the brain of the asphyxiated newborn human infant as it has been shown to do in the neonatal guinea pig.[2]

Summary

Cardiac activity was maintained for 21 hours in an apneic 580-Gm. (1.25-lb.) female fetus. During this period, the fetus was perfused with 300 ml. of oxygenated blood and kept at deep colonic temperatures between 22 C and 0.1 C. For more than 17 hours the temperature was below 15 C, and for nearly 2½ hours it was below 1 C. On five occasions the temperature was reduced to 4 C or less, and during the last two cooling periods it reached 0.1 C.

Electrocardiograms showed that heart activity did not cease until the temperature fell to 0.1 C and that it recommenced spontaneously on rewarming. A comparison of the records at 11 C showed that after the periods of deepest hypothermia there was an increase in the height (increase in voltage) and a narrowing (increase in rate of ventricular depolarization) of the QRS complex. This was most striking after the first cooling period, when the QRS complex reached a maximum of 1 mv. However, even after the fifth period 0.5 mv. was recorded. At the beginning of the study the voltage was 0.01 mv. at 25 C.

This appears to have established a record both for the lowest temperature during which cardiac activity has been recorded and the lowest temperature from which spontaneous recovery of heart beat has been observed. Also established is a record for the longest time during which heart beat has been reported in a perfused human fetus. This shows that the heart of the premature infant will tolerate far wer temperatures than previously thought ossible.

This study was aided by grants from the National Institutes of Health and Association for the Aid of Crippled Children.

Dr. John Lind provided material and facilities for this study.

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RING DERMATITIS.—During the past five years, many patients have been patch-tested with metals. Every so often there would be seen a dermatitis of the ear lobes, back, neck, chest, shoulders, wrist, or lower abdomen where metal contact presupposed a metal sensitivity. The diagnosis seemed so obvious that it was recorded. When patch tests were performed, the diagnosis was not confirmed. A greater range of test solutions were made up, and these, too, failed to confirm the presence of any metal sensitivity. Patch tests were done adjacent to the area of dermatitis without positive results. Testing solutions were dropped on the patch of dermatitis without the slightest indication of an aggravation. It thus seems that a dermatitis from contact with metal, in the presence of negative patch-test results, may well be a primary irritation from the action of skin-surface salts on metals and/or alloys.—L. E. Gaul, M.D., Ring Dermatitis, *A. M. A. Archives of Dermatology,* May, 1958.

EFFECT OF TRANQUILIZING AGENTS ON RADIOACTIVE IODINE UPTAKE IN THE THYROID GLAND

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There are many patients who arouse clinical suspicion of having hyperthyroidism yet who do not suffer from true thyrotoxicosis. These patients usually have no enlargement of the thyroid gland and lack the true eye signs of toxic diffuse goiter (Grave's disease). They are nervous and insomnic, complain of palpitation of the heart, and have some degree of tachycardia. They may or may not show evidence of weight loss and may even be obese. A routine study of 24-hour uptake of radioactive iodine (I^{131}) by the thyroid gland in these persons will often show an uptake which is in the upper normal or even in the toxic range.[1] Further studies may reveal normal thyroid function by means of such tests as conversion ratios (ratio of inorganic to organic iodine in plasma) and plasma protein-bound iodine studies. It has been shown that oral administration of thyroid extract or triiodothyronine will reduce the I^{131} uptake in persons without true thyrotoxicosis but will not greatly affect the I^{131} uptake in persons with hyperthyroidism. According to Selye,[2] stimulation of thyroid activity during periods of stress and by the stress mechanism are readily postulated. It was felt that this increase in thyroid activity might be reflected in an increase in the I^{131} uptake. It was therefore decided to test the effect of tranquilizing agents on those patients in whom elevated I^{131} uptakes were found without clinical signs of hyperthyroidism and to measure changes, if any, in the I^{131} uptake by the thyroid gland.

Methods

Patients recently seen who had had I^{131} uptake determinations which were higher than the expected normal range were requested to return for repeat examination. Those patients who volunteered to return and who were selected for this study in each case showed an elevated I^{131} uptake when the test was repeated. Determination of the protein-bound iodine to inorganic iodine ratios revealed, however, that the conversion from organic to inorganic iodine in each patient was less than 50%, thus establishing that hyperthyroidism probably was not present. A double-blind study was then carried out with three-week courses of therapy with meprobamate (Miltown), 400 mg. three times a day; meprobamate, 400 mg. fortified with 0.5 mg. of benactyzine hydrochloride three times a day; and a placebo tablet which was indistinguishable from the other two tablets. The investigators knew which was the meprobamate but not which was the meprobamate with benactyzine and which was the placebo. In so far as possible, the three groups of medicaments were administered in rotation so that each patient received all three courses of medication, but in varying order. After each course of medication, the I^{131} uptake determination was repeated.

Results

The results of the investigation are set forth in the accompanying table. Twelve patients were subjected to either the whole or a part of the study. The initial I^{131} uptake varied from 35 to 62% in these patients. All of the patients were women, with one exception. One patient failed to respond to treatment with the tranquilizing agents and continued to show an increase in I^{131} uptake during the course of management. This patient had had an initial conversion ratio of 46%. After three months the conversion ratio had risen to 76% and the I^{131} uptake to 63%. At this time it was felt that a diagnosis of true hyperthyroidism had to be made, and the patient was treated subsequently with I^{131}, to which she responded very well. (This case is not included in the table.)

Thyroid Radioactive Iodine (I^{131}) Uptake in Response to Treatment with Tranquilizing Agents

		24-Hr. Uptake, %			
Case No.*	Age, Yr.	Initial	After Placebo	After Meprobamate	After Meprobamate and Benactyzine
1	30	62	34		20
2	58	46	37	30	28
3	20	52	58		
4	51	49	49	41	
5	49	42	36	7	9
6	40	38	53		
7	41	35	35	35	35
8	50	41		32	
9	20	41		35	
10	25	56	48		28
11	26	62	43	40	23
12	41	62			38
Av.		49	44	33	26
Median		49	43	35	28

* All patients were female except that in case 12.

Nine patients did not respond to the medication with the placebo, and the I^{131} uptake was either materially unchanged or higher after completing the medication for three weeks with the placebo tablets. In two patients the administration of placebo tablets had to be discontinued since the patients did not feel that any improvement was being obtained from them. The response to the meprobamate alone in eight patients was generally satisfactory, although in three instances the reduction in I^{131} uptake was not considered to be significant.

From the Isotope Laboratory, Mercy Hospital.

In six patients the response to the meprobamate and benactyzine combination was extremely satisfactory. There was reduction of the I^{131} uptake in almost each instance to below 30%. Interesting was the case of the male patient who had been treated two years prior to this study for true hyperthyroidism with radioactive iodine. After this treatment he had remained well for a period of two years, at which time he returned because his symptoms of nervousness and his "jittery" state were similar to what he had experienced while suffering from thyrotoxicosis. His I^{131} uptake, which had been followed closely during the past two-year period, had ranged around 40%. At the time of the study it had risen to 63%. After a three-week course of meprobamate plus benactyzine, the I^{131} uptake fell to 38% and there was no subjective evidence of nervousness or other symptoms of excitement.

Comment

From these results it appears evident that the tranquilizing agents can reduce the I^{131} uptake of the thyroid gland. The locus of this effect, of course, was not established by this study. There is no reason to suspect that it is due to a direct chemical effect on the thyroid gland, such as occurs with the antithyroid drugs (thiouracils), nor does the effect seem to be similar to that of administered thyroid extract, with which there is a reduction of I^{131} uptake by the thyroid gland in those patients in whom true clinical hyperthyroidism does not exist. The reaction of the tranquilizing agents indicate that meprobamate shares the central interneuronal blocking action of mephenesin but has an action of much longer duration.[3] The drug appears to be a mild hypnotic and tolerance does not appear to develop. Addiction and toxicity have been reported to be low.

The in situ action in the central nervous system is not yet understood, although it appears to be useful in the treatment of alcoholism and anxiety and tension states. It is possible that the reduction of the tension state would have some secondary or other effects on the demands on the thyroid gland, such as in the stress mechanism as postulated by Selye.[2] However, confirmation exists that the tranquilizing agents do not have an effect on the activity of the thyroid gland in the presence of true hyperthyroidism or thyrotoxicosis. There is no reason to suspect that the effect on the thyroid gland could be produced by the small doses of I^{131} administered in the tracer tests, which would total less than 100 μc for each patient.

Summary

In a group of patients in whom the radioactive iodine (I^{131}) uptake was elevated without clinical evidence of hyperthyroidism and in the absence of enlargement of the thyroid gland but in whom there were signs of nervousness and excitement which exist in a chronic tension state, the effect of tranquilizing agents on the uptake of I^{131} was studied. The results in 12 patients who were subjected to a double-blind study indicate that tranquilizing agents, particularly meprobamate plus benactyzine hydrochloride, may sufficiently reduce the effect of tension or anxiety mechanisms on the endocrine system to effectively decrease the thyroid activity as measured by the uptake of I^{131}.

104 S. Michigan Ave. (3) (Dr. Friedell).

The meprobamate used in this study was supplied as *Miltown* by Wallace Laboratories, New Brunswick, N. J.

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RHEUMATIC FEVER AND THE WILLOW TREE.—Therapeutic advances are *seldom* the product of logical reasoning. They are more commonly the result of haphazard empiricism, often based on false assumptions. The use of salicylates in the treatment of rheumatic fever by Maclagan in 1876—a story Langdon-Brown enjoyed telling, for it appealed to his sense of the ironic—is the classic example of how progress in treatment is made. Maclagan believed that, in the orderly Victorian universe in which he lived, the natural remedy for each disease was to be found where that disease was prevalent. Noting the frequency both of rheumatic fever and of the willow tree in marshy country, he was led to use the salicin obtained from the second in the treatment of the first. After the first empirical leap in the dark, progress comes from working backwards, analyzing the reasons for success, and building upon this more solid foundation. It will be seen that the chemotherapy of malignant disease is following this traditional pattern, and its theoretical basis is largely derived from a rationalization of its successes.—R. B. Scott, D.M., F.R.C.P., The Chemotherapy of Malignant Disease, *British Medical Journal,* Jan. 4, 1958.

ACUTE BLOOD LOSS REQUIRING FIFTY-EIGHT TRANSFUSIONS

USE OF ANTIGRAVITY SUIT AS AID IN POSTPARTUM INTRA-ABDOMINAL HEMORRHAGE

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and
Donald F. Dohn, M.D., Cleveland

In this case of placenta percreta (a placenta that has grown through the uterine wall because of failure of development of decidua basalis), control of bleeding was finally accomplished after a desperate struggle in which the application of pneumatic pressure to the lower half of the body appeared to mark the turning point.

The modified antigravity suit (commonly referred to as the "G-suit") used in this case was developed primarily for the purpose of preventing postural hypotension during neurosurgical operations with the patient in the sitting position.[1] It consists of a large plastic inflatable bladder that is wrapped about the lower half of the body after the manner of a huge blood pressure cuff. This principle was first employed in 1903 by Crile[2] for the prevention and treatment of hemorrhagic shock in surgery of the head and neck. As blood transfusions became relatively safe it was abandoned, to be reapplied many years later in the era of high-speed flying.

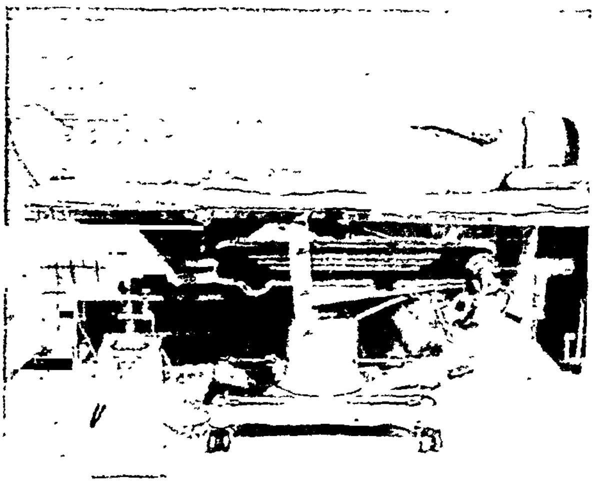
Report of a Case

A 36-year-old woman, gravida 6, para 3, in her sixth month of pregnancy, was delivered of a stillborn fetus while she was under spinal anesthesia. Delivery was followed by a frightening gush of blood and an immediate state of shock. Manual exploration revealed the upper half of the placenta to be completely detached from the anterior uterine wall, while its lower half, extending downward to the internal os, was tightly adherent. The separated part of the placenta was removed manually and efforts to separate the adherent portion were abandoned when it became apparent that this was an instance of placenta percreta. The uterus was firmly packed, fluids were administered intravenously, and a blood transfusion was given. The patient rallied as preparations were being made for an abdominal hysterectomy.

The abdominal cavity was opened by lower midline incision with the patient under cyclopropane anesthesia. An area 20 cm. in diameter involving the anterior wall of the lower uterus resembled the fetal surface of a placenta. The intrauterine pack was removed per vaginam and the patient again went into shock. It was decided that hysterectomy should be performed immediately, and as the bladder reflection was incised, placental tissue was encountered. There was no anterior uterine wall, the placenta having completely invaded and replaced the myometrium, and there was no cleavage plane between placenta and bladder. Hysterectomy was followed by troublesome bleeding from the remaining placental tissue, finally controlled by figure-of-eight sutures, oxidized cellulose (Oxycel), and the pressure of the advancement of the bladder over this oozing area. Closure was completed four hours post partum, by which time the patient had received 11 units of blood and 3,000 ml. of 5% dextrose in water. With phenylephrine (Neosynephrine) hydrochloride added to the intravenously given fluids, the blood pressure was 110/50 mm. Hg and the pulse rate was 130.

Despite the continued intravenous administration of citrated blood and of fluids containing vasoconstrictor agents, the blood pressure gradually fell to 70/60 mm. Hg. The abdomen became distended and tympanitic; respiratory embarrassment and ashen pallor ensued. It seemed obvious that massive intra-abdominal hemorrhage had occurred.

Seven hours after hysterectomy the abdomen was reopened. An estimated 3,500 ml. of clotted and liquid blood was removed from the peritoneal cavity, 1,000 ml. of which was filtered and retransfused. With the table in the shock position, the patient was receiving infusions of blood or fluid into four veins simultaneously. The chief sources of bleeding appeared to be the spongy mass of placental tissue beneath the bladder, the stumps of the broad ligaments, round ligaments and tubes. These were quickly religated with figure-of-eight sutures, the pelvis was packed, and a unit of blood was given into the aorta. With removal of the packs, bleeding continued. The right internal iliac artery was tied off, temporary ligatures were placed on both common iliacs, and the pelvic and vaginal packs were reapplied, but to no avail. As the patient was receiving approximately her 30th transfusion, the rate of bleeding increased and hemolysis became evident by inspection of the urine. In an attempt to restore platelets and other elements lost from the circulation, the patient was given 2 units of fresh blood by direct transfusion, 3 units of fibrinogen, a unit of serum albumin, 3 Gm. of calcium gluconate, and hydrocortisone.



G-Suit is placed beneath the patient, folded over him, and laced snugly. Gas enters through a tube at one end. Desired pressure is maintained by escape valve shown hanging from table. This is filled with water to desired level. This pressure cannot be exceeded as excess gas escapes by bubbling through water.

From The Cleveland Clinic Foundation and The Frank E. Bunts Educational Institute.

After six hours of operating time the prognosis appeared hopeless. Therefore, nine large packs were placed in the peritoneal cavity, the incision was closed snugly over them, and the patient was returned to her bed. Sand bags were placed on the abdomen, the legs were wrapped with elastic bandages, and the foot of the bed was elevated on shock blocks. Within 18½ hours of delivery, the patient had received 55 units of blood, which included the 2 units recovered from the peritoneal cavity and the 2 units of uncitrated platelet-containing blood given by direct transfusion. While 2 additional units of citrated blood were running in, the blood pressure taken with the patient in the shock position was 86/62 mm. Hg and the pulse rate was 144.

At this juncture, in an effort to accomplish more effective compression of the bleeding area, the G-suit was wrapped about the patient so as to encompass her from the ankles to the epigastrium and was inflated to 20 mm. Hg. The patient aroused and complained of her head-down position as the blood pressure rose to 104/72 mm. Hg. The shock blocks were removed and the pressure fell to 96/76. The rate of transfusion was slowed and the pressure gradually rose to 114/80 while the pulse rate increased to 160. Twenty-four hours post partum, after the administration of one additional unit of blood, the pulse rate began to decrease. The 24-hour output of urine was 415 ml. Thirty-six and one-half hours after delivery, and after the patient had been in the G-suit for 18 hours, the blood pressure stabilized at 130/78 mm. Hg, and the pulse rate at 130. Six hours later the G-suit was deflated and removed with no significant change in the pulse rate or the blood pressure.

Eighty-three hours after delivery the abdomen was opened for the third time, a quantity of blood was evacuated, and the abdominal and vaginal packs were removed. This was followed by no further bleeding, and the vital signs remained stable. The subsequent hospital course was marked by ileus, pulmonary atelectasis, fever, jaundice, and a left subphrenic abscess. The patient was discharged on the 54th hospital day; subsequent convalescence was uneventful except for a mild episode of hepatitis which developed on the 129th day. There were no cerebral symptoms at any time aside from a mild instability on walking, which cleared completely within six months.

Comment

When the G-suit was applied 18½ hours post partum, after two lengthy and apparently futile abdominal operations, the patient had received 10,000 ml. of fluid with other restorative measures, and was receiving her 56th and 57th units of blood. During the first few hours in the G-suit she received 1 additional unit of blood, making a total of 58 units within 24 hours. No more blood was needed. Among the many doctors who attended this patient, there is some division of opinion as to whether the final control of bleeding was due chiefly to the use of the G-suit, the intra-abdominal packs, the 2 units of fresh uncitrated blood, or to prayer.

The patient's blood was type O, Rh+ and she received only type O, Rh+ donor blood throughout the ordeal. The supply of banked blood was rapidly exhausted in this emergency and thereafter the citrated blood that she received, still warm from the donor, probably contained a goodly number of platelets. She was given 29,000 ml. of blood within 24 hours. To our knowledge this is the largest quantity ever administered within this period of time. Artz, Sako, and Bronwell[3] have reported a Korean battle casualty to whom 23,350 ml. of blood was given within 24 hours.

As a result of the above experience, the G-suit was used in another case of postpartum hemorrhage in which 20 transfusions were required within 20 hours to combat hemorrhagic shock. In this case also, after application of the G-suit, only 1 additional unit of blood was required to restore and maintain the blood pressure level.

2020 E. 93rd St. (6) (Dr. Gardner).

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THERAPEUTIC USE OF CORTICOTROPIN AND CORTICOIDS.—In the presence of any inflammatory or allergic reaction that proves limiting to the well-being, activity and long-range plans of the patient, the use of corticoids or corticotropin should be considered. However, at all times one must remember that corticoid therapy is only symptomatic and that its effectiveness is due largely to inhibiting the bodily defense mechanisms and minimizing their immediate and long-range destructive effects. As the body defenses are, of course, in general beneficial, such therapy is always a calculated risk and the indications are only relative. Only in substitution therapy is there an unequivocal indication. Here one attempts to reproduce physiologic levels of corticosteroids when the adrenal cortices are not functioning normally, rather than to produce pharmacologic effects by corticoid levels in excess of normal. In all other conditions one must weigh the benefits derived from the partial control of the manifestations of a given disease with the inevitable side effects that accompany the use of these agents when used for their pharmacologic effect.—V. C. DiRaimondo and P. H. Forsham, Pharmacophysiologic Principles in the Use of Corticoids and Adrenocorticotropin, *Metabolism,* January, 1958.

FATAL JAUNDICE ASSOCIATED WITH IPRONIAZID (MARSILID) THERAPY

REPORT OF A CASE

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Iproniazid, a derivative of isoniazid, has recently been introduced as a "psychic energizer." The drug was originally investigated for its antituberculous properties, but the central nervous system stimulation noted in many patients, greater than that obtained with the parent compound, led to its present use. A number of neurological and autonomic disturbances, mostly relatively mild, have occurred in many patients receiving the drug and have been well described.[1] A more serious and less well-known toxic effect of the drug is its action on the liver.

Abnormal liver function test results, developing in the course of iproniazid therapy, were reported in 9 out of 52 patients in whom such tests were done.[2] All returned to normal on the same, or decreased, dosage or on withdrawal of the drug. Out of another group of 30 patients receiving iproniazid,[3] 3 developed transient sulfobromophthalein (Bromsulphthalein) retention. In a series of 142 patients treated with the drug,[1] 4 developed jaundice, all with subsequent recovery. Of these patients, the jaundice of one was in all probability due to anatomic factors unrelated to iproniazid therapy; since the other patients had all received multiple transfusions, a clear-cut relationship to the drug could not be definitely established. A fifth case of jaundice, ending with a fatal necrosis of the liver, has recently been reported in one patient of a series of 31 receiving the drug,[4] and we are aware of another patient who became jaundiced and died shortly after stopping a two-month course of therapy with the drug, and who, on postmortem examination, showed a generalized necrosis of the liver.[5] This case occurred in a large hospital in New York City, and exposure to other known hepatotoxins, including contaminated blood, could reasonably be excluded. It is the purpose of the present paper to present another case of fatal jaundice in association with iproniazid therapy.

A 47-year-old male was first seen in this hospital on Dec. 2, 1957, presenting with the picture of jaundice and hepatic coma. His history included a myocardial infarction three years earlier, with frequent chest pain since, for which he had been treated with a variety of coronary vasodilators, the most recent having been pentaerythritol tetranitrate and choline theophyllinate. He had had vague intermittent epigastric distress for a long time, for which he had been given antispasmodics, but he had never had any documented gastrointestinal tract pathology (except for a rectal polyp removed two months previously). There was no history of allergies, of jaundice, or of known hepatic or renal disease. His alcoholic intake had always been low, and he had had no blood transfusions. For over a year prior to his present illness he had been nervous and depressed and had been treated with a variety of sedative and tranquilizing drugs, including phenobarbital, reserpine, perphenazine (Trilafon), and chlorpromazine. He had taken no chlorpromazine for at least six months prior to his present illness, according to his local physician. All other drugs except the coronary vasodilators were discontinued about two and a half months prior to admission, at which time he was started on therapy with iproniazid, 150 mg. per day. He was instructed to reduce this dosage to 100 mg. or less in a few weeks, although his compliance with this instruction is uncertain, since he found the drug so beneficial in alleviating depression. He stated that no other drug had given him an equal sense of well-being, a condition which lasted, under continuous treatment with iproniazid, until two weeks before admission, when he began to be aware of anorexia and fatigue. He went to his local physician, who could find nothing unusual, and specifically no enlarged liver. Four days later the patient noted dark urine and early signs of jaundice. These symptoms were followed in a day or two by frequent, nonbloody vomiting, dull pain in the right upper quadrant, and progressive weakness. One week before admission he had a palpable, tender liver, with obvious jaundice, 4+ cephalin flocculation, 4+ thymol turbidity, and normal alkaline phosphatase and cholesterol levels. Shortly before admission it had become impossible to feel the liver, and the patient had become more deeply jaundiced, markedly drowsy, and at times disoriented.

On admission to the hospital the patient was a well-developed, somewhat obese male, extremely jaundiced, somewhat confused, and frequently disoriented. His temperature was 98.6 F (37.0 C), pulse 86, respirations 14, and blood pressure 110/70 mm. Hg. The remainder of the physical examination was normal. There was no tremor, and the liver was not palpable.

Laboratory results were as follows: The hematocrit was 52%, the hemoglobin level 17.2 Gm. per 100 cc., the white blood cell count 19,400 per cubic millimeter (polymorphonuclear leukocytes 80%, lymphocytes 16%, monocytes 3%, and basophils 1%), and the platelets were diminished, as seen on a smear. The urine was dark brown and strongly positive for bile, with a specific gravity of 1.012, albumin 1+, glucose 1+, with two to three red blood cells and two to three white blood cells per high-power field, and occasional granular bile-stained casts. The erythrocyte sedimentation rate was 3 mm. per hour, and the carbon dioxide content of the blood was 12.8 mEq. per liter. The sodium content of the blood was 141 mEq. per liter and the potassium and chlorine content 4.9 and 103 mEq. per liter respectively. The blood sugar level was 89 mg. per 100 ml., blood urea nitrogen level 13 mg.%, prothrombin time 29

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seconds (normal is 15 seconds), cephalin flocculation and thymol turibidity both 4+, and the bilirubin level 30.4 mg.% (direct). The total cholesterol level was 83 mg.% (19% esterified), and the serum ammonia concentration was 140 mcg.%. The patient's blood culture was negative. Gastric aspiration yielded 4+ blood by the guaiac test. A chest x-ray made with a portable machine was normal. The electrocardiogram showed evidence of an old posterior myocardial infarct.

Despite intensive therapy with intravenously given fluids, antibiotics, and finally steroids, the patient had a rapidly downhill course with fever, tachycardia, increasing disorientation, hypotension, and finally death 24 hours after admission. His serum ammonia level rose to 364 mg.% preterminally.

At autopsy the patient was found to have a normal-sized liver, which on microscopic section showed massive necrosis of liver cells, with some preservation of architectural framework. The sinusoids were congested, especially about the central veins, while the bile ducts were normal. Inflammatory cell infiltration, predominantly of the chronic variety, was noted, together with areas of regenerating liver and bile duct cells. The kidneys were congested and edematous and showed focal hemorrhages into the pelvic fat. An occasional distal convoluted tubule showed early necrotic changes, and several bile plugs were noted in the tubules. The stomach contained some gross blood but was normal on gross and microscopic section. The heart showed evidence of an old posterior infarct of the left ventricle. The remainder of the examination, including that of the central nervous system, was essentially normal.

Comment

A 47-year-old man who had been on therapy with iproniazid, 150-100 mg. a day, for about two and one-half months died with fulminating jaundice and the picture of acute yellow atrophy of the liver. The only known hepatotoxic drug he had received, chlorpromazine, had been withdrawn six months previously. It is not claimed that iproniazid was definitely the toxic agent, since this illness could have represented an infectious hepatitis. It is also possible, though unlikely, that an injection with a poorly sterilized needle at the time of his rectal polypectomy two months previously could have transmitted serum hepatitis. Nevertheless, it is noteworthy that iproniazid has been associated with transient abnormalities of liver function in a moderate number of patients in whom these tests were made, that one case of death due to necrosis of the liver in a patient receiving the drug has already been reported, and that another unpublished case is known to exist. The jaundice appears to be a hepatocellular, rather than an obstructive, type. Serious consideration should be given to this potentially severe form of toxicity in a relatively new drug.

620 W. 168 St. (32).

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ANTIMETABOLITES AS DRUGS.—The introduction of the antimetabolite concept into pharmacology seems to be causing such a change in thinking about the mode of action of drugs that a revolution may be said to be in progress. Perhaps one of the most significant aspects of this revolution is that reliance on chance for the discovery of the first member of a new series of useful agents is being broken. It is now becoming possible to predict the chemical structure of the first member of a new series and to see these predictions come true. This is not to say that the end of chance discovery and of empiricism is just around the corner. Many more great discoveries will undoubtedly be made this way in the future, just as they have been made in the past. . . . What has been added by the antimetabolite concept is the knowledge of how to interpret a chance discovery of this sort and how to proceed to the next logical step. The antimetabolite concept depends for any of its successes on the accumulated knowledge of fundamental physiology and biochemistry. We must know what substances are important in particular bodily functions. We must know what the signs of deficiency of each of these essential metabolites are. Also, in the present state of infancy of the concept, we must often rely on a lucky conjecture. We must feel, therefore, that all reliance on chance has not been discarded but that we have been able to advance a little way.—D. W. Woolley, Ph.D., M.D., The Revolution in Pharmacology, *Perspectives in Biology and Medicine,* Winter, 1958.

PERIVENTRICULAR CALCIFICATION AND CYTOMEGALIC INCLUSION DISEASE IN NEWBORN INFANT

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and
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The purpose of this case report is to call attention to the unusual findings on the skull roentgenograms of a newborn infant. The films disclosed calcium lining the walls of the lateral ventricles of the brain. Such a picture has been reported four times previously,[1] all in infants with generalized cytomegalic inclusion disease. Our patient showed the characteristic cells of cytomegalic inclusion disease in the urine. We are presenting this case to suggest that this radiographic finding, when present, indicates a diagnosis of cytomegalic inclusion disease and may be pathognomonic of the disease.

Report of a Case

History.—An infant (fig.1) was born July 17, 1957, after a 40-week gestation. He weighed 2,154 Gm. (4.7 lb.) and therefore was transferred to the premature nursery at the Jackson Memorial Hospital for care. He was the first child of a 20-year-old primipara whose blood was group A and Rh positive and whose serologic test for syphilis was negative. The mother was born and reared in Puerto Rico. The pregnancy had been uneventful, with a normal spontaneous delivery. The infant cried spontaneously at birth but was noticed to have a small head.

Physical Examination.—At the time of the initial examination the infant was active, with a good color and a high-pitched cry. He was not icteric, and no petechiae or ecchymoses were seen. The calvaria appeared small in relation to the face and the size of the body. The bones of the calvaria overlapped slightly, and both fontanels were small. The anterior fontanel was 1 cm. in diameter and the posterior was 0.5 cm. in diameter. The skull failed to transilluminate. The eyegrounds were normal. The lungs were clear, and the heart was normal. The liver was palpable 2 cm. below the right costal margin, but the spleen was not palpable.

Laboratory Data.—The hemoglobin level was 18.0 Gm. per 100 cc. The white blood cell count was 11,100 per cubic millimeter; a differential count showed 11% band cells, 30% polymorphonuclear cells, and 59% lymphocytes. Lumbar puncture (fluid taken at the time the pneumoencephalograms were done) yielded crystal-clear cerebrospinal fluid that contained 14 cells, all mononuclear; a protein level of 149 mg.; and a sugar level of 36 mg. per 100 ml. A colloidal gold curve was 000121000. The serologic test for syphilis was negative. Sabin-Feldman dye tests done on two occasions, two months apart, on the mother's and infant's serum, were negative. These were done by the Communicable Disease center, Chamblee, Ga.

Roentgenograms of the skull showed a marked microcephalia. The bones of the calvaria overlapped. There was an unusual layer of calcification following the outline of the ventricles. No other calcification was noted. Pneumoencephalograms (fig. 2) demonstrated that the calcium deposits were periventricular and that there was marked dilatation of the lateral ventricles.

A disintegrated cell with changes indicative of those seen in cytomegalic inclusion disease was found in the urinary sediment. In order to obtain more material, a 24-hr. specimen was collected in formalin (10 ml. of formalin [37-40% formaldehyde] for each 100 ml. of urine). The entire 24-hr. specimen was centrifuged, and the sediment was smeared on clean glass slides. These preparations were stained with Harris' hematoxylin–alcoholic eosin. By this means, clear-cut examples of cells (probably from renal tubules) containing intranuclear inclusions and showing nuclear changes typical of cytomegalic inclusion disease (fig. 2, *insert*) were found. No cytoplasmic inclusions were seen.

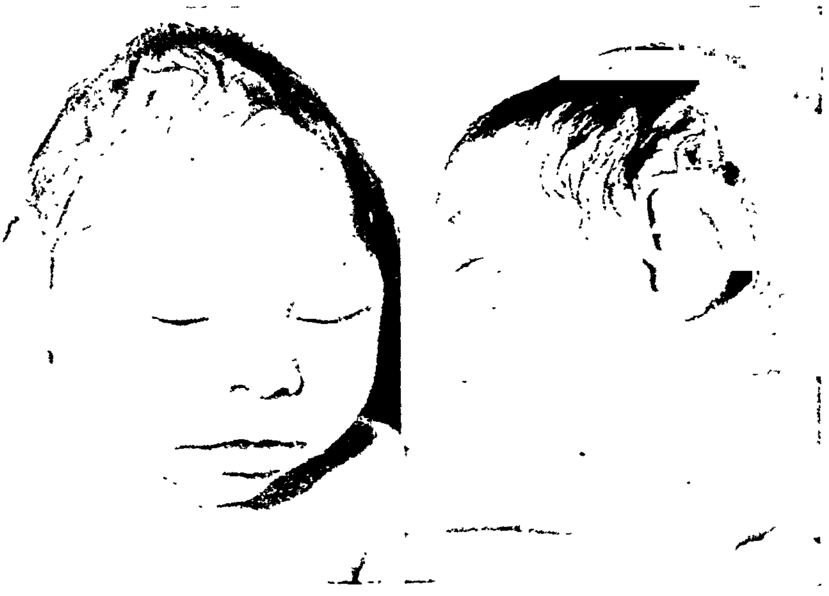
Fig. 1.—*Left*, anteroposterior view of infant's head showing small calvaria and overlapping of sagittal suture. *Right*, lateral view of infant's head showing small calvaria.

Viral isolations were attempted from urine and mucous membrane washings from the mouth by Dr. M. Sigel, of the Virology Laboratory at the University of Miami, Coral Gables, Fla., but were unsuccessful. Complement-fixation antibody determinations were done by Dr. T. H. Weller of the Harvard School of Public Health, Boston, and by Dr. W. P. Rowe, of the National Institutes of Health, Bethesda, Md. At neither institution were the studies conclusive for the disease.

From the departments of radiology, pediatrics, and pathology of the University of Miami School of Medicine, and the sections of radiology, pediatrics, and pathology of Jackson Memorial Hospital.

Course.—The infant was discharged from the hospital at one month of age, weighing 2,500 Gm. (5.5 lb.), with a diagnosis of cytomegalic inclusion body disease. During his stay in the hospital he showed no evidence of jaundice or bleeding tendencies. His eyegrounds, examined at the time of discharge, revealed no evidence of chorioretinitis. His spleen was never palpable, but his liver was still 2 cm. below the right costal margin.

At 2 months of age he was readmitted to the hospital for follow-up studies. His weight was 4,255 Gm. (9.4 lb). The calvaria remained obviously small in relation to the size of the body. The sutures no longer overlapped, and there was no evidence of his developing a hydrocephalus. The hemoglobin level was 9.9 Gm. per 100 cc. without evidence of bleeding. The liver was palpable 1 cm. below the right costal margin. The spleen was not palpable. His urine sediment was reexamined for cytomegalic inclusion bodies, but none could be demonstrated on this admission. Repeat roentgenograms of the skull showed essentially the same pattern of calcium formation as was noted two months previously, at birth.

At 4 months of age, the infant began having generalized convulsive seizures and was readmitted to the hospital. The seizures were easily controlled with phenobarbital. Repeat roentgenograms of the skull showed a calcium formation in the periventricular areas similar to that noted at the time of birth. Intranuclear cytomegalic inclusion bodies could not be demonstrated in his urinary sediment on this admission. The infant has subsequently required phenobarl to control his convulsive seizures and is consid mentally retarded.

Comment

The antemortem diagnosis of cytomegalic inclusion disease has been aided by various means: the recognition of the typical cells in hematoxylin-and-eosin or Giemsa-stained urine,[2] gastric washing,[1d] lung tissue,[3] and spinal fluid[4]; viral isolation from urine,[5] aqueous of the eye,[1d] and liver biopsy specimens[5a]; and complement-fixation[5b] and neutralization studies.[5a] The finding of the typical cells in the urine is inconstant as shown in our case and one other.[1d] The virus isolation, complement-fixation, and neutralization studies are difficult to perform, not generally available, and of varying success. The limitations of the above diagnostic aids lend emphasis to the value of a characteristic radiographic picture that may be present in some cases.

If the infant survives, the enlargement of the ventricles could result in dispersal of the calcium so that its periventricular location is no longer apparent. In such a case, the calcium could assume a "snowflake" appearance indistinguishable from the appearance of toxoplasmosis.[6] The finding of the calcium within the subependymal white matter . .' matrix of the lateral ventricles with sparing of

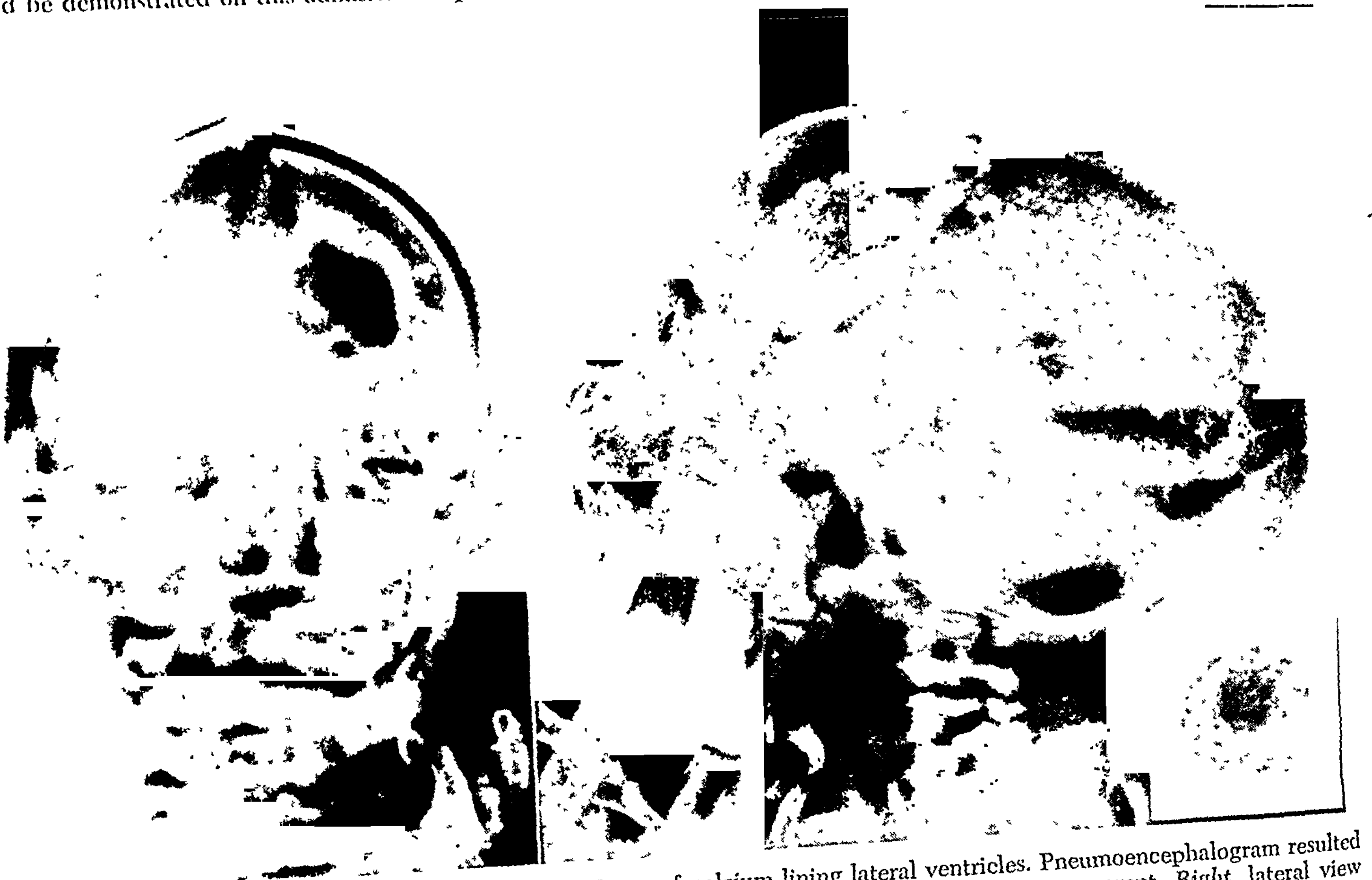

Fig. 2.—*Left*, anteroposterior view of skull showing layer of calcium lining lateral ventricles. Pneumoencephalogram resulted in filling of left lateral ventricle with air, thus making periventricular location of calcium more apparent. *Right*, lateral view of skull showing small calvaria, overlapping sutures, and periventricular calcium. *Insert*, cell, stained with Harris' hematoxylin—alcoholic eosin stain, containing intranuclear inclusion and showing nuclear changes typical of cytomegalic inclusion disease. The large dark inclusion is surrounded by fragmented chromatin.

the remaining ventricular system may reflect the intrauterine age at which the disease occurred.[1b] The periventricular matrix of the lateral ventricles is still active in the late intrauterine and early neonatal life, whereas the matrix of the remaining ventricular system has reached maturity by the third month. Perhaps the disease is not contracted until after the third intrauterine month and the immature cells are most susceptible to invasion by the virus.

Summary

A case of advanced periventricular calcification in a newborn infant has been studied. Such a finding appears to be characteristic of cytomegalic inclusion disease and when present should suggest this diagnosis.

1700 N. W. 10th Ave. (36) (Dr. Daurelle).

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ACUTE INTESTINAL OBSTRUCTION.—This is the commonest serious surgical condition met with in general hospitals as emergency and taxes the surgical team to its utmost. One is confronted with a grave condition, and the entire resources of the team are required to treat the patient. It is to be noted that this otherwise fatal condition is supremely amenable to timely surgical intervention, although the incidence of mortality is still high due to poor communication, ignorance, poverty and fear causing considerable lapse of time before the patient reaches the hospital, leading to delay in diagnosis and early treatment. . . . The characteristic triad of pain, vomiting and progressive distention is almost always present, the duration varying from a few hours to a few days and in general denotes the severity of obstructive mechanisms. Absolute constipation may be an early or late sign, and may be occasionally misleading. Recurrent intestinal spasms with inability to pass flatus is almost certainly due to obstruction. In a doubtful case, positive diagnosis can be established by x-ray investigations and the approximate site of the lesion determined. . . . Intestinal intubation properly done will reduce the mortality rate particularly in the presence of adhesive obstruction. However, there is a danger in persisting with this therapy when surgical intervention is imperative. The absolute contraindications of the use of long intestinal tubes are strangulating obstruction of the small bowel and any obstruction of the large bowel. . . . The main step is the relief of obstruction by cutting the band or untwisting as the case may be. In all cases where the gut is not viable, resection and anastomosis is undertaken if the patient's condition permits. . . . Generally speaking, the patients settle down within 48 hours. A mild degree of paralytic ileus persists for 24 to 48 hours in cases of resection. Gastric suction and intravenous fluids are maintained till normal bowel movements are established. Blood transfusions are of very great value and is the best aid in correcting hypoproteinæmia and anæmia.—V. D. Kirpekar, M.S., F.I.C.S., Acute Intestinal Obstruction. *Journal of the Indian Medical Association*, April 1, 1958.

TIMESAVING AID IN HIP-PINNING

F. K. Holzwarth, M.D., Rochester, N. Y.

Anything which will facilitate the accurate and fast placing of the initial guide-wire for a Smith-Petersen nail is surely a boon, especially in poor-risk patients. For some time, it has been my custom to insert a Michel clip, after reduction and skin preparation, over the midpoint of the head of the femur.

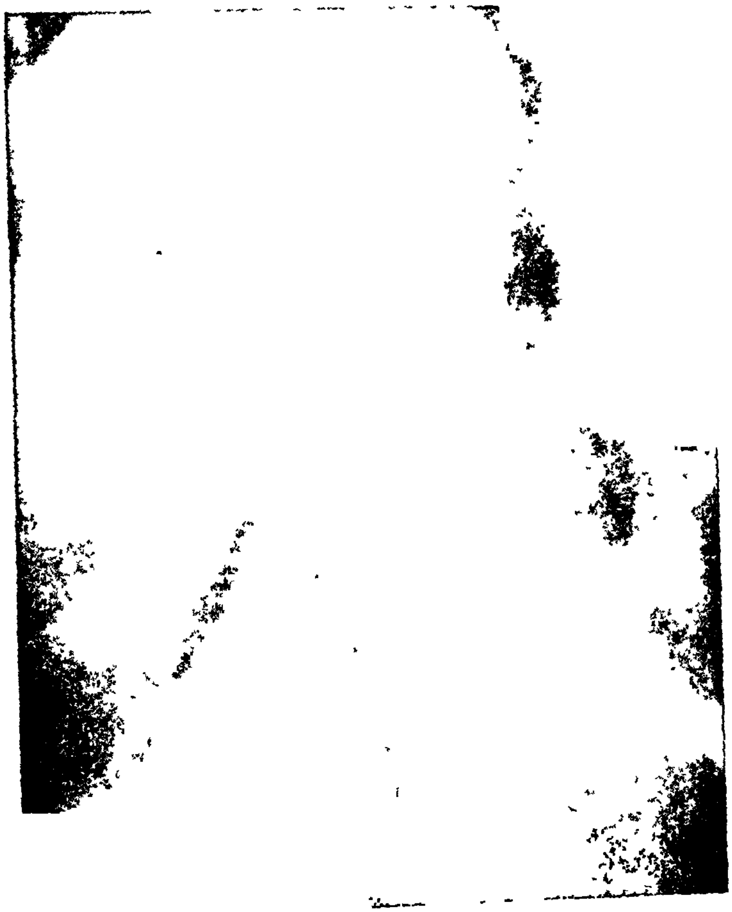


Fig. 1.—Anteroposterior roentgenogram showing guide wire lying on the skin between three Michel clips.

This point is located by palpating the femoral artery where it crosses the inguinal ligament, then moving vertically down for 1 in. and laterally for 0.5 in. Two additional clips are inserted, 0.5 in. medially and laterally to the first respectively. Ordinarily, a check x-ray is then done to ascertain the accuracy of the reduction. If it is satisfactory, the usual lateral incision and insertion of the initial guide-wire follows. The clips, plainly visible on the film, afford a target toward which to aim the drilled wire.

Frequently, the first guide-wire is not found in optimum position by x-ray. A second wire must be inserted and another x-ray taken. This consumes from 5 to 10 minutes. It has seemed possible that the time required for inserting the initial "sounding" wire might be saved by sliding a guide-wire in the loops of two clips, the one over the femoral head and the other placed at a point on the skin about 0.5 in. below the base of the trochanter major. A third clip may be added between these two to anchor the wire more securely. This wire will lie on the skin in an axis closely paralleling the midline of the femoral neck. The anteroposterior view serves as a guide in angling the first wire to be drilled into the femur and as an indicator of the depth desired to bring the point 0.25 to 0.5 in. short of penetrating the head.

The length of wire protruding lateral to the femur is then measured; the balance of the wire represents the correct length of the pin. The skin-wire is now pushed up through the clips until its distal end is just below the lateral clip. Its pointed end will be out of the way over the lower part of the abdomen.

If the wire thus lying on the skin appears to be in suitable position, a guide wire parallel to it is drilled through the neck to the proper depth in the head. All that remains is to drive the Smith-Petersen nail over it. If the skin wire is slightly misangled (in obese patients its proximal end will be angled anteriorly when it is pushed over the abdomen), the drilled wire can be inserted at the corrected angle. Thus, it is often possible to reach a suitable position with the first guide wire drilled. This technique has been used in 35 cases and has proved to be a rational, timesaving measure.

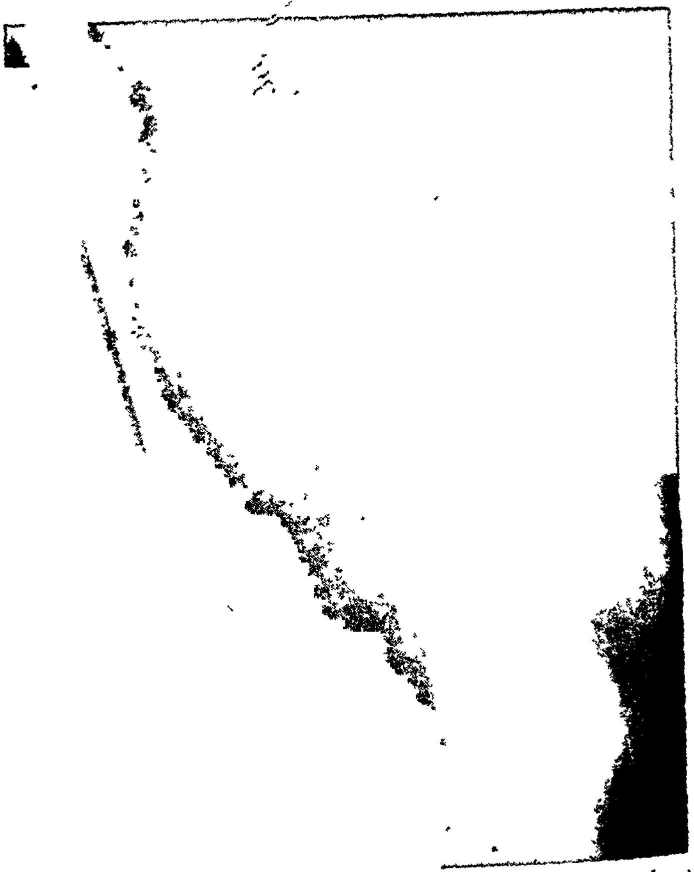


Fig. 2.—Lateral roentgenogram showing skin wire about 3 in. anterior to the femur and nearly parallel to the neck.

13 S. Goodman St. (7).

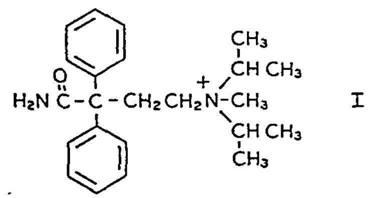
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Drugs are based on the evaluation of available scientific data and reports of investigations.

H. D. Kautz, M.D., *Secretary.*

Isopropamide Iodide.—(3-Carbamoyl-3,3-diphenylpropyl)diisopropylmethylammonium iodide.—The structural formula of isopropamide iodide may be represented as follows:



Actions and Uses.—Isopropamide iodide, a synthetic anticholinergic compound, produces the peripheral effects of atropine and the belladonna alkaloids. Although it is chemically classified as a quaternary ammonium compound, the drug does not elicit sympathetic ganglionic blocking effects except at doses greatly in excess of therapeutic levels. Isopropamide differs from other anticholinergics chiefly with respect to duration of action. Since the drug apparently possesses an inherently prolonged action, antisecretory and spasmolytic effects can be maintained with the administration of single doses at intervals of 12 hours. It is useful as an adjunct to the management of peptic ulcer and other conditions of the gastrointestinal tract that are characterized by hypermotility and hyperacidity. Side-effects referable to therapy with isopropamide are those of anticholinergics in general and include dryness of the mouth, blurring of vision, and difficulty in urination. The drug is contraindicated in patients with glaucoma, prostatic hypertrophy, obstruction at the bladder neck, stenosing peptic ulcer, or pyloric or duodenal obstruction.

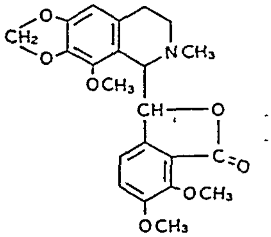
Dosage.—Isopropamide iodide is administered orally. Dosage should be adjusted to the needs of the individual patient as determined by clinical response and appearance of side-effects. The usual dose for adults is 5 mg. every 12 hours.

Preparations: tablets 5 mg.

Applicable commercial name: Darbid.

Smith, Kline & French Laboratories cooperated by furnishing scientific data to aid in the evaluation of isopropamide iodide.

Noscapine.—2-Methyl-8-methoxy-6,7-methylenedioxy-1-(6,7-dimethoxy-3-phthalidyl)-1,2,3,4-tetrahydroisoquinoline.—The structural formula of noscapine may be represented as follows:



Actions and Uses.—Noscapine is one of the isoquinoline alkaloids of opium. Except for morphine, it is the most abundant of the opium alkaloids, occurring to the extent of 6% in the seed capsules of Papaver somniferum. Because of its derivation from the opium poppy, the drug was formerly known as narcotine and was employed empirically in the past as an analgesic, hypnotic, and sedative. More recent evidence has shown that the drug bears little similarity, either chemically or pharmacologically, to morphine or the narcotic alkaloids of opium; hence, it has been renamed noscapine.

Noscapine shows papaverine-like effects on smooth muscle, causing coronary vasodilation in animals and, in large enough doses, bronchodilation. In man, there are no marked symptoms after administration of moderate doses. The drug produces none of the usual opiate-like effects such as constipation, miosis, blood pressure changes, and respiratory depression. Analgesia, hypnosis, and sedation are negligible or nil. Noscapine is rapidly absorbed from the gastrointestinal tract. Little is known about its metabolic fate or excretion.

The pharmacological action upon which the clinical use of noscapine is based resides in its ability to suppress the cough reflex in experimentally induced cough in animals and human volunteers and in patients with respiratory disease. The drug reduces the frequency and intensity of coughing paroxysms. Its antitussive potency under these experimental conditions is approximately equal, milligram for milligram, with that of codeine, both drugs having approximately the same onset and duration of action. In humans, clinical experience with the drug in cough of pathological origin has not been sufficiently extensive to establish its final status.

Therapeutically effective doses of noscapine are essentially devoid of the unpleasant side-effects of codeine, and, except for occasional instances of nausea (which rarely proceed into vomiting), its side-effects are negligible. As with any antitussive agent, it should not be given in situations in which retention of respiratory secretions or exudates may be harmful.

Although noscapine is an opium alkaloid within the scope of the Harrison Act, it is exempt from requirements for order by prescription under certain conditions. However, experiments have shown that moderately large doses have no morphine-like effects in former addicts and no ameliorating effect on the severity of the morphine abstinence syndrome. Further, virtually no tolerance to the antitussive effect of the drug has been demonstrated. Hence noscapine is, for practical purposes, without addicting liability.

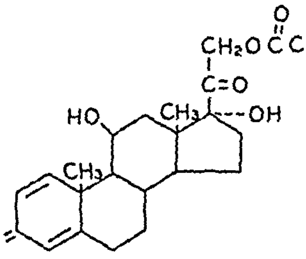
Dosage.—Noscapine is administered orally. The usual dose is 15 to 30 mg. given three or four times daily.

Preparations: powder (bulk).

Applicable commercial name: Nectadon.

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of noscapine.

Prednisolone Butylacetate.—Prednisolone *tert*-butylacetate.—$\Delta^{1,4}$-Pregnadiene-3,20-dione-11β,17α,-21-triol *tert*-butylacetate.—The structural formula of prednisolone butylacetate may be represented as follows:



Actions and Uses.—Prednisolone butylacetate, a very slightly soluble ester of prednisolone, is suitable for intrasynovial and soft tissue injection. The drug appears to have a slightly greater potency and a longer duration of action than the acetate or butylacetate esters of hydrocortisone. It is useful for the treatment of those painful disorders of the joints, tendons, and bursae which are usually responsive to local glucocorticoid therapy (injection). Since the drug is so slightly soluble, 24 to 48 hours may elapse after injection before relief of symptoms becomes significant. The duration of relief varies from patient to patient but averages from two to three weeks. A continuation or even an increase in local discomfort (postinjection flare) may occur and be present for several hours after the administration of prednisolone butylacetate; however, this is usually followed by effective relief of pain and improvement in local function. Systemic steroid effects are not a problem when therapeutic doses are employed; with higher dosage, mild transient subjective improvement of joints remote from those injected has been reported. (See the general statement on glucocorticoids in New and Nonofficial Drugs.)

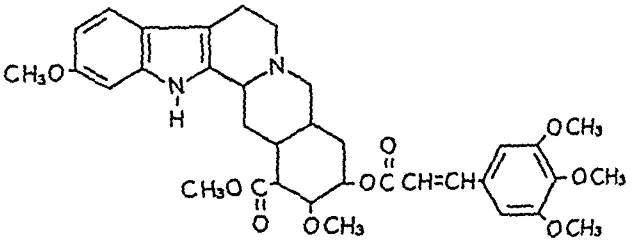
Dosage.—Prednisolone butylacetate is administered by intrasynovial or soft tissue injection *only*; it should not be given by any other route. The usual techniques governing intrasynovial (intraarticular and intrabursal) injection should be observed, and a 22-gauge or larger needle should be employed. The injection site may be infiltrated with a local anesthetic if necessary. Dosage and interval between injections depend on size of joint, degree of inflammation, and individual response of the patient. For large joints such as the knee, the usual dose is 20 to 30 mg.; in smaller joints, 7.5 to 10 mg. may be sufficient. A dose of 20 to 30 mg. is usually employed for the treatment of most forms of bursitis. The suggested dose for inflammatory conditions of the tendons is 4 to 10 mg. For the treatment of ganglion, 10 to 20 mg. is injected directly into the cyst cavity.

Preparations: suspension (injection) 20 mg. in 1 cc. and 100 mg. in 5 cc.

Applicable commercial name: Hydeltra-T.B.A.

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of prednisolone butylacetate.

Rescinnamine.—3,4,5-Trimethoxycinnamic acid ester of methyl reserpate.—The structural formula of rescinnamine may be represented as follows:



Actions and Uses.—Rescinnamine, a purified ester alkaloid of the alseroxylon fraction of species of Rauwolfia, is closely related in chemical structure and pharmacological action to reserpine. Thus, rescinnamine is useful for the management of mild, labile hypertension and as a tranquilizing agent in agitated patients with simple neuroses and frank psychoses. While clinical experience with rescinnamine is not as extensive as that with reserpine, most observations indicate that both drugs are of approximately the same order of effectiveness.

Although all the side-effects and toxic reactions that occasionally follow the administration of reserpine have been reported after therapy with rescinnamine, the incidence and severity of some of these may be less with the latter agent. Sedation and bradycardia, in particular, appear to occur less frequently and in milder form with rescinnamine. The incidence of other side-effects such as weakness and fatigue, nasal congestion, dizziness, confusion, increased appetite, and weight gain is about the same with both agents; in some patients, the severity of these effects may be slightly less with rescinnamine than with reserpine. Both drugs should be used with the same precautions, and both are subject to the same contraindications. (See the monograph on reserpine in New and Nonofficial Drugs.)

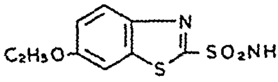
Dosage.—Rescinnamine is administered orally. For the treatment of mild hypertension or simple neuroses, initial doses of 0.5 mg. twice daily for two weeks have been employed. Thereafter, daily dosage requirements are either reduced or increased by increments of 0.25 mg., depending on therapeutic response and appearance of side-effects. While information available to date is not adequate to establish the dosage of rescinnamine for the treatment of institutionalized psychotic patients, daily amounts ranging from 3 to 12 mg. have been employed, apparently with satisfactory results.

Preparations: tablets 0.25 mg. and 0.5 mg.

Applicable commercial name: Moderil.

Pfizer Laboratories, Division of Chas. Pfizer & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of rescinnamine.

Ethoxzolamide.—6-Ethoxy-2-benzothiazolesulfonamide.—The structural formula of ethoxzolamide may be represented as follows:



Actions and Uses.—Ethoxzolamide is a diuretic agent with actions and uses similar to those of the chemically related sulfonamide compound, acetazolamide. Both drugs are potent inhibitors of carbonic anhydrase and are believed to influence fluid mobilization by the same basic mechanism of action. Therapy with either results in alkalinization of the urine and a mild degree of metabolic acidosis. Available evidence indicates that the initiation of diuresis may be achieved with smaller doses of ethoxzolamide than of acetazolamide. On a weight basis, ethoxzolamide appears to be approximately twice as active as acetazolamide. Both have approximately the same duration of action, the effects lasting about 8 to 12 hours after a single oral dose.

Ethoxzolamide is used to produce diuresis in patients with mild to moderate congestive heart failure. It may also be used in conjunction with mercurial diuretic agents for the treatment of the more severe forms of heart failure. Such combination therapy may permit a reduction in the dosage and frequency of mercurial administration; in certain cases, it may even be possible to eliminate the need for the mercurial diuretic.

Ethoxzolamide decreases intraocular pressure by inhibiting the formation of aqueous humor. It is, therefore, useful in the treatment of glaucoma, particularly acute glaucoma. The drug is usually not employed alone but is given concomitantly with cholinergic miotics because such therapy appears to be additive. The long-term effectiveness of carbonic anhydrase inhibitors remains to be established.

Ethoxzolamide has been employed to reduce the incidence of convulsive attacks in epileptic patients subject to grand mal and petit mal seizures. Although beneficial effects have been reported in certain cases, there is insufficient evidence to establish the usefulness of the drug as an antiepileptic agent.

In general, ethoxzolamide appears to be well tolerated. The most commonly reported side-effects include nausea, dizziness, and numbness and paresthesias of the fingers and toes or at the mucocutaneous junctions of the lips or anus. Other less frequently reported reactions include drowsiness, fatigue, headache, and dryness of the mouth. Long-term therapy, such as is employed in chronic glaucoma, may lead to anorexia and weight loss. Side-effects generally subside or disappear with a reduction in dosage.

Ethoxzolamide should be used cautiously in patients with hepatic cirrhosis, since it may induce episodes of disorientation. The drug is contraindicated in patients with renal failure, hyperchloremic acidosis, Addison's disease, and in any condition in which sodium and/or potassium levels are depressed.

Dosage.—Ethoxzolamide is administered orally. For diuresis in mild to moderate congestive heart failure or in combination with mercurial diuretics in severe heart failure, a single dose of 62.5 to 125 mg. is given in the morning after breakfast for three consecutive days of each week; this dose may also be given on alternate days. In resistant cases, single doses of as much as 250 mg. may be required. For use in glaucoma, the dosage ranges from 62.5 to 250 mg. two to four times daily, depending upon the individual response in intraocular pressure. As is true for acetazolamide, the administration of ethoxzolamide should be intermittent rather than continuous. Dosage for the prophylaxis of epileptic seizures is not established, but daily amounts up to 750 mg. have been employed.

Preparations: tablets 125 mg.

Applicable commercial name: Cardrase.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of ethoxzolamide.

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PERINATAL MORTALITY AND MORBIDITY

DEATH is associated with birth and being born in the United States more often than it is with any disease except heart disease, cancer, and cerebral hemorrhage." With this Dr. Martha M. Eliot introduces her paper (see this issue, page 945), on Deaths Around Birth—The National Score. Accompanying Dr. Eliot's paper is one by Drs. Baumgartner and Pakter "assessing the local situation" and a third by Drs. Verhoestraete and Puffer presenting "a world view." The significance of the above quoted statement is attracting the attention of many in the medical and public health research field. Dr. Eliot expresses the tragedy involved in this loss of life as well as in the morbidity that too often accompanies child bearing and being born. The morbidity, or aftermath as it is sometimes called, is represented by the survival of infants with such conditions as cerebral palsy, epilepsy, mental retardation, and congenital malformations.

In assessing the local situation Drs. Baumgartner and Pakter recall the concerted attack on maternal mortality following a study made in 1933 and published by the New York Academy of Medicine. The report of that study indicated that two-thirds of the maternal deaths in New York City were then considered preventable. The effect was the establishment of city and county medical society committees to review and study all maternal deaths. By 1945 the maternal death rate was decreased to what was earlier thought to be the irreducible minimum. Ten years later, however, this "irreducible minimum" had been reduced by 70%. Although many other factors contributed to this dramatic reduction in maternal mortality, awareness of the problem and concerted efforts in its solution were certainly not the least. The authors show the relative lag in reducing infant mortality; this lag is especially evident when the early neonatal deaths (hebdomadal) are considered. In New York City the death rate during the first seven days after birth was 17.7 per 1,000 live births in 1955, compared to the relatively only slightly higher rate of 20.2 per 1,000 live births in 1937. Some of the factors responsible for this lag are suggested and some of the known remedial procedures are outlined. The need for more and better research on these problems is emphasized. A recent study indicating that many of these deaths of newborn infants are preventable has stimulated the formation of county and city perinatal mortality study committees and the organization within many hospitals of regular perinatal mortality conferences. Drs. Baumgartner and Pakter indicate that "much benefit is bound to accrue when the combined efforts and interest of the various groups are focused on a common aim of increasing knowledge concerning causes of death and preventing needless loss."

Presenting a world view, Drs. Verhoestraete and Puffer have observed that over a 40-year period the over-all infant death rate has declined rapidly in, for example, the United States, Sweden, and the Netherlands but that the decline in the neonatal and fetal death rates in these countries has been slower. In fact, the statistics indicate that within the early neonatal period in these years the death rate has remained almost constant. The importance of perinatal mortality (defined here as early neonatal and late fetal) as a major problem of wastage of life in technically developed countries is emphasized. The differences in perinatal mortality rates for countries of various stages of technical and socioeconomic development are outlined, as are many interesting relationships relative to causes of mortality in these countries. Drs. Verhoestraete and Puffer conclude that "an intensive program of research for the prevention of those conditions that determine the size of perinatal mortality rates appears, at present, necessary. The discovery of adequate preventive measures not only would allow further reduction of the perinatal problem in highly developed countries but might prove more generally applicable in technically less developed areas than programs of specialized care which are too costly and require too highly specialized skills and facilities to have any real effect within the low priority for program planning that can be given them at the present time."

These three articles serve well to point up the various aspects of and the many factors involved in the problems of perinatal mortality and morbidity. Because perinatal mortality and morbidity have been reduced remarkably in some areas of highly favorable circumstances in the United States and other countries as well, it is apparent that perinatal casualties could be reduced considerably if present knowledge of prevention were more widely and intensively applied. The necessity for more research is recognized, of course, in order that methods will be discovered for preventing deaths and morbidity from causes not now precisely known. Several questions concerning a concerted attack on the problems of perinatal mortality and morbidity are raised. Some of these are concerned with the need for more uniformity of terms and *definitions; for more coordination of specialties and* scientific disciplines in the clinical and public health approaches to study and research; for clarification and better recording of causes of death; for better pathological study; and for ways and means to reach those socioeconomic groups needing service but sometimes not seeking it and other times not knowing of its availability. And of especial interest is the emphasis that the above papers have placed on the morbidity aspects of conditions involving the perinatal period. This has been referred to as a "continuum of reproductive casualty."

It is with these problems and questions in mind that the Committee on Maternal and Child Care of the American Medical Association's Council on Medical Service is devoting its time and efforts. Through regional and other meetings, through research and study of present programs, and through publications, the committee is attempting to stimulate interest in and disseminate information on these problems of the perinatal period to the end that present knowledge will be utilized effectively. An example of this effort is the forthcoming series of articles to appear in THE JOURNAL entitled Study of Perinatal Mortality and Morbidity Programs in the United States. Simultaneously the committee is developing a Guide for Study of Perinatal Mortality and Morbidity that will be designed to assist state and county medical societies, state and local health departments, and community hospitals in their efforts to reduce deaths and the long-term illnesses resulting from conditions of the perinatal period.

CHANGING ASPECTS OF ENVIRONMENTAL HEALTH

There has always been change but in many fields the tempo of current changes has been greatly increased.[1] Environmental health measures were formerly concerned mostly with living micro-organisms and their living vectors. They must now include nonliving long-range stresses. The development of large metropolitan areas extending far beyond city boundaries has brought with it problems of coordinated control and cooperative effort. It is estimated that over 50% of the population in the United States now lives in such metropolitan areas. With this increase in urbanization more attention must be paid to air pollution, the conservation and treatment of water supplies, and the disposal of domestic and industrial wastes including the recent and ever-increasing problem of radioactive wastes. Noise and the increasing pace of life with mounting internal tensions and mounting accident rates, especially those connected with traffic, are also problems awaiting solution.

It has been said that human beings can adjust to any environment on earth, whether it be physical, chemical, microbial, or social, but this is true only within certain limits. In the past changes usually came about slowly enough to give man a chance to adjust gradually. Now that changes are occurring so fast it is becoming more and more evident that technological advances will have to be adapted to the capacity of the people to cope with the resultant environmental changes rather than that people will have to adjust to more rapid changes. Margins of safe tolerance will have to be determined.[2] This is an almost virgin area of research. Once determined, means of keeping environmental stresses within safe bounds must be found. The time is rapidly approaching when these problems must move beyond the conference stage. Concrete actions will have to be taken. Appropriate actions cannot be taken unless there is a greater public awareness of the nature, magnitude, and urgency of the problem. The cooperation of industry is necessary if we are to anticipate and prevent tragedies such as the fatal smog of 1948 in Donora, Pennsylvania, rather than to try to correct conditions after great damage has been done.

Speaking of the mental health aspects of rapid urbanization and the attendant problems already enumerated, Porterfield[2] points out modern man's need for more time for reflection and more chance for individual self-expression. The Brickdust Row of the near slums of O. Henry's time has been replaced by the prefabricated housing developments found in many modern suburbs, but the effect is the same. An atmosphere of monotony and regimentation is created and with it an aftermath of emotional frustrations and psychosomatic complaints in adults and delinquent behavior in youth. The environment must express not repress the individual.

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[1] Hollis, M. D.: Environmental Health Aspects of Future Metropolitan Area Complexes, Am. J. Pub. Health 48:454-455 (April) 1958.

[2] Porterfield, J. D.: Mental Health in the Environment of the Metropolitan Area of the Future, Am. J. Pub. Health 48:489-494 (April) 1958.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Recently, leafing through an anthology of famous speeches, I lingered over Patrick Henry's deathless words on American liberty. I was struck by the realization that the evils against which he inveighed and the objectives which he so vehemently urged are substantially the same as those which confront us today. The choice which he was called upon to make challenges us today. In his ringing words, "The question before the House is one of awful moment to this country. For my part I consider it as nothing less than a question of freedom or slavery."

In their day, our forefathers strove to wrest their freedom from an alien government which, in defiance of the will of the people, sought to restrict and usurp the rights of the individual for the exaltation of the power of the few who typified the state. In our day, we are called upon to preserve that freedom against a threat which arises out of the tyranny of our own despotic selfishness.

If we proceed upon the misleading but appealing assumption that democracy is a system under which whatever the majority wants is good and whatever is good we are all entitled to have, then the road to national ruin will be paved by the indulgence of ill-considered and selfish desires.

Democracy is the most exacting and difficult of all systems of government because it demands of all citizens intelligence, integrity, and unselfish devotion. It asks most of us to be better than we are, *but not better than we could be.* It invites the lowliest to aspire to greatness, because no man can become great who does not serve a cause or an ideal more important than himself.

President Eisenhower sounded a note of warning for us all in his last address on the State of the Union. He declared: "Freedom has been defined as the opportunity for self-discipline. Should we persistently fail to discipline ourselves, eventually there will be increasing pressure on government to redress that failure. By that process freedom will step by step disappear."

That is why the members of the medical profession—alarmed more as thinking citizens than as physicians—look with suspicion and fear upon legislation which, in utter disregard of economic facts, promises nebulous mass benefits at the cos of essential, individual dignity and freedom. Tha is why we of the medical profession favor the utilization of voluntary means for the solvent individual citizen to defray the costs of the services and benefits which he chooses to enjoy.

We are convinced that programs which involve more and more taxation to pay for benefits made impartially available to all persons—in disregard of their individual need of such benefits or of their ability to provide them for themselves—are a threat to the character and freedom of our nation.

The end-result of such programs, we believe, will inevitably be the exaltation and expansion of the powers and rights of the state and the diminution and ultimate usurpation of the powers and rights of the individual citizens.

We physicians contend that it is the right and the duty of the individual American citizen, so far as he is able, to provide for himself and his dependents. We contend that his earnings should not be so drained off in soaring taxes as to make him no longer independent and self-sustaining. We contend that any program—at any level—which tends to do this is not only destructive of the character and status of the citizen as a free man but destructive of the character of our government.

This I believe and this I will defend as one who has had the distinct honor and privilege of serving as the one hundred eleventh President of the American Medical Association.

David B. Allman, M.D.
Atlantic City, N. J.

ORGANIZATION SECTION

STATEMENT REGARDING FHA-INSURED LOANS BEFORE A SENATE SUBCOMMITTEE BY R. B. ROBINS, M.D.

May 21, 1958

Mr. Chairman and Members of the Subcommittee:

I am Dr. R. B. Robins, a practicing physician of Camden, Arkansas. I am testifying today at the request of the chairman of the board of trustees of the American Medical Association, and I am pleased to give you the views of the American doctors on some of the problems of caring for our aged citizens. I am a past vice-president of the A. M. A. and past president of the American Academy of General Practice.

My testimony today will be concerned with the medical problems that are peculiar to the aged, the facilities available to care for their ordinary housing needs as well as their medical needs, the cost of these services, and the role of the proprietary nursing home in helping to solve some of these problems.

It is our understanding that the Federal Housing Administration presently is offering mortgage insurance for construction of large nonprofit institutional-type homes for the aged which may have a section for those needing nursing care.

My remarks today will be directed solely toward pointing out the need for a similar program of loan guarantees for proprietary as well as nonprofit organizations. I want to point out that currently 71% of nursing home patients are cared for in proprietary institutions.

As the basis for my testimony, I want to state that the American Medical Association, through its Board of Trustees, has approved and will support a government-insured loan program of the FHA type for nongovernmental hospitals and nursing homes whether their ownership is of a nonprofit or a proprietary character.

In recent years, the problems of the elderly have attracted an ever-increasing amount of national attention, both within the government and among groups and associations outside government. This is understandable since the proportion of our population over age 65 is increasing at a rate that might be described as amazing. In 1900 there were only 3,000,000 of these elderly citizens. Now there are approximately 15,000,000. Already they represent nearly nine per cent of our entire population, and the trend has not yet leveled off.

Not one but many factors explain how mankind has been extending its life span—advances in medical science, a new awareness of the principles of nutrition, better working conditions that allow more men and women to reach retirement age and better housing. All of these factors and others have contributed to the increased longevity of our population.

New problems naturally attend such gains, many of which can only be solved by persons skilled in furnishing medical care and nursing services.

From its beginning more than a century ago the American Medical Association has been deeply involved in medical aspects of caring for the aged. At work now in this field are three active committees attached to the Association's Council on Medical Service. They are the Committee on Aging, the Committee on Indigent Care and the Committee on Medical and Related Facilities.

Our work in these fields has been performed in cooperation with other interested agencies. In 1946, representatives of the A. M. A. met with representatives of the American Hospital Association, American Public Health Association, and the American Public Welfare Association, to establish the Interim Committee on Chronic Illness which, in May, 1949, was changed to The Commission on Chronic Illness, with representatives of the general public, industry, labor, agriculture, education, religion, social sciences, journalism, health, and welfare.

A number of studies were made. One of these I will leave with you, entitled "Nursing Homes, Their Patients, and Their Care," published by the U. S. Public Health Service which cooperated in this study.

Although the Commission was disbanded as such in June, 1956, the cooperating organizations continue to work on the parts of the program in which they are best qualified. The Council on Medical Service of the American Medical Association still prints the Newsletter on Chronic Illness, a copy of which is attached.

This interest of the A. M. A. continues right down the line to the family physician who is on the scene when the various medical crises occur in the lives of older people. A majority of our constituent state medical societies have formed committees on aging and are making their contributions. In addition, as a recent development, a series of regional meetings, sponsored by the A. M. A., has been held to stimulate local action in bringing the best possible medical care to senior citizens in their homes, in physicians' offices, in nursing homes and in hospitals.

I would like to mention several other concrete achievements that are the result of cooperative undertakings of the medical profession, the hospital and nursing home people, the insurance industry and the drug industry.

First, new treatment and surgical procedures have been developed to ease the discomforts of the ill and disabled aged, and in many cases to rehabilitate them to the point where they can take care of themselves and often return to employment. Some examples of this are cortisone, antibiotics, tranquilizers, early ambulation of operative cases, physical and occupational therapy, early evaluation of seriously ill and injured for vocational guidance and training.

Second, enrollment of older people under voluntary health insurance has increased at an encouraging rate in recent years. It has gone up about 100 per cent in the last seven years alone. Presently, exclusive of the approximately 3,000,000 older persons who receive public assistance, more than 50 per cent of those over 65 have some form of health insurance.

Third, the American Medical Association has joined with the American Hospital Association, the American Dental Association and the American Nursing Home Association in the formation of the Joint Council to Improve the Health Care of the Aged. The council's long-range goal is better health for all the aged. Its most immediate concern is working out answers to meet the financial and social problems that accompany chronic illness.

Fourth, hospitals are actively experimenting with gradations of care, a new concept that attempts to fit the patient to the type of care he needs, but not for complete hospital care when that is not required.

Fifth, for the last year, representatives of the American Medical Association and the American Nursing Home Association have been meeting regularly to prepare improved medical care standards for the nursing homes, standards that admittedly are badly needed in some sections of the country.

In February of this year the first national conference on nursing homes and homes for the aged was held here in Washington. I offer for the record a summary of that conference's report, containing information supporting our request for action in this field.

Most of the aged ill or disabled can, and are, best cared for in the physician's office or in their homes, still others require care in a medical facility. The question is, do these people need care in a general hospital at a cost of $20 to $25 per day? Some of them do, but others could receive the maximum professional attention their condition calls for in a less expensive facility—a properly constructed and operated nursing home, with professional medical and nursing care at hand or readily available. I am speaking now of older people with conditions that are chronic, such as . . . hypertension, diabetes, arthritis, paralysis of extremities.

There is a much larger group who require some nursing and medical care, and who could be provided for quite satisfactorily in private homes. Yet, for many reasons, the relatives—if there are relatives—are not in a position to take in these older people. They need housing, and some medical care, but not hospital care in many cases. Yet, many thousands of them are in hospitals, merely because there are not suitable nursing homes or other chronic disease facilities.

This situation points up the critical need for new and improved facilities tailored to the specific health requirements of the older citizens. Nursing home administrators have appeared before your committee earlier. They have convincing evidence, accumulated over recent years, that they can not provide the services they want to provide in quality or in quantity because they are unable to obtain the credit they need on reasonable terms.

The normal lending agencies just are not making loans to proprietary nursing homes in any significant volume. The lenders have their reasons—because the homes generally are one-purpose structures, unattractive as a straight commercial risk, even though foreclosures are rare.

As doctors we know the need for attractive, clean, safe nursing homes, where we can be sure our older patients will receive the proper nursing care under our direction, and where the costs will not be prohibitive.

Through Hill-Burton and other programs th federal government for years has been assistin public and nonprofit hospitals through mone grants. The proprietary nursing homes are not asking grants, but only a federal guarantee to make possible for them to obtain the mortgages the need. They will pay the going rate of interest i cluding the mortgage insurance premium and w repay the loans.

We strongly urge this committee to consider an insured type loan for which proprietary and nonprofit nursing homes could qualify, under FHA. This would stimulate the local lending agencies and bring about an atmosphere that would produce the capital needed for construction and equipment.

I do not know of a single group in the medical field that does not now urge the construction of special facilities for the chronically ill and for the aged. That is exactly what a well-equipped, well-administered nursing home is. All medical authorities with whom I have been in contact believe this to be one of the really critical medical shortages today.

LETTER REGARDING POSITION OF ASSISTANT SECRETARY OF DEFENSE

May 13, 1958

Honorable Carl Vinson
Chairman, Armed Services Committee
House of Representatives
Washington 25, D. C.

Dear Mr. Vinson:

The American Medical Association has been following with a great deal of interest the public hearings currently being conducted by the Armed Services Committee of the House of Representatives relative to the reorganization of the Department of Defense.

The Association has demonstrated for more than a century its sustained interest in seeing that the best available medical services are provided for our Armed Forces in time of war or peace. In recent years, since the enactment of the National Security Act of 1947, the Association has been instrumental in presenting, to both the legislative and executive branches of government, the need for health and medical policy coordination at the highest level of our government. The first Hoover Commission in 1948 recommended that strong control over military medical policy be exercised from the level of the Secretary of Defense.

In July, 1949 the position of Assistant to the Secretary of Defense for Health and Medical Affairs was established, and in 1953 this position was changed to that of Assistant Secretary of Defense (Health and Medical). Through the operations of this office and with the cooperation of the Surgeons General of the various branches of the Armed Forces an enviable record of increased efficiency and economy has been established.

Since the establishment of this position the military medical services have experienced the lowest case fatality rates of any military service in peace or wartime. At the same time, the military medical services have maintained the highest effective rate of any military service, even though in many instances American Armed Forces were serving in disease ridden areas throughout the world and under the most hazardous conditions of peacetime and wartime. Furthermore, the military medical services established the first unified supply procurement agency of the Armed Forces, which with a Department of Defense blood program, reaching to our world-wide military outposts, proved highly efficient during the Korean campaign.

Joint utilization of military medical facilities, educational programs, military logistics, including patient evacuation, intelligence and operations, and research and scientific developments have also been made possible under the directorship of the civilian Assistant Secretary of Defense (Health and Medical) and his predecessors. The interservice use of military medical facilities, including hospitals and dispensaries, as well as the interservice staffing of military hospitals has been accomplished by programs directed from this office.

During the Korean Conflict, this office of the Department of Defense directed the coordination of medical and health liaison with the Forces of the United Nations, and this has been continued with the NATO and SEATO Forces. During this same period, this office established the first interagency medical council, responsible for the coordination of the federal medical effort on behalf of our wartime and peacetime missions of health and medical care.

Experience has clearly shown that as a result of the respect and authority vested in an Assistant Secretary of Defense it is possible for him to formulate policy and direct the programs of the military medical services of the Department of Defense, while at the same time commanding the respect of his opposite numbers in the highest circles of our own government, in foreign governments and in the professional and scientific as well as lay national and international groups.

We know that the prestige of the military medical services has increased since establishment of this office both in this country and abroad, particularly in the eyes of civilian medicine.

In summation, we believe, therefore, that it is in the best interests of the Armed Forces, the military medical services, and our country that the position of Assistant Secretary of Defense for Health and Medical Affairs be maintained in the Department of Defense organization with a civilian physician appointed to this position.

Sincerely yours,
F. J. L. Blasingame, M.D.
General Manager

A. M. A. LEGAL CONFERENCE FOR MEDICAL SOCIETY REPRESENTATIVES

A panel discussion on the legal aspects of medical practice through "third party" mechanisms involving some hospitals, closed panels, medical schools, and management and union health plans occupied a full day's session in Chicago, in May, for 150 medical society representatives. It was the second legal conference to be sponsored by the Law Department of the American Medical Association—attracting executive secretaries, attorneys, and consultants from 35 states and the District of Columbia.

Discussing the medical care program of the United Mine Workers of America welfare fund, Arthur H. Clephane, legal counsel for the Medical Society of the State of Pennsylvania, said: "The profession everywhere must sit down with the U. M. W. A. and with all leading third parties across the conference table as men of good will and develop a plan for working together which will insure the best quality of medical care to the third party beneficiaries which is reasonable and fair to the funds and to the doctors."

John Lansdale Jr., legal counsel for the Cleveland Academy of Medicine, speaking on "Hospitals and the Practice of Medicine," said: "Medical practice is basically medical judgment, and not the technique or effort specifically or in itself." Francis Shackelford, special counsel for the Medical Association of Georgia, reported details of a recent cooperative agreement reached by organized medicine in Georgia with the University of Georgia School of Medicine, relating to faculty treatment of fee-paying patients at the university's Talmadge Memorial Hospital. After a special committee of officials from the A. M. A. and the Association of American Medical Colleges visited the school to resolve differences, a spokesman said: "It may well be that this committee has established a precedent which may prove quite beneficial in the resolution of similar situations."

Legal aspects of membership in county medical societies were discussed by Eugene R. Warren, counsel for the Arkansas Medical Society. The panel moderator, A. Leslie Hodson, a Chicago attorney who acts as an A. M. A. consultant, commented: "Extreme care should be taken by local societies in rejecting applications for membership or disciplining an existing member simply and solely because he is a member of a closed panel." Charles Margett, legal counsel for the Medical ciety of Queens, reported on "Closed Panel es of Practice."

Other Program Topics

May 10, the second day of panel sessions, in J. Holman, of the A. M. A. Law Department, related results of a national survey on professional liability; Jule M. Hannaford, counsel for the Minnesota State Medical Association, discussed "Hospital Records and Tissue Committees," and Jake Hunt, counsel for the Oklahoma State Medical Association, reviewed "Group Programs and Professional Liability Insurance Review Committees." Attorney Don H. Reuben of Chicago discussed libel, slander, and privacy in medicine, A. M. A. Attorney Bernard D. Hirsh reported on "Tax Advantages of Corporations and Unincorporated Associations," and Robert Throckmorton, counsel for the Iowa State Medical Society, spoke on legislation and lobbying practices of state medical societies.

Welcoming and introductory comments were delivered to the conference by A. M. A. President David B. Allman, A. M. A. General Manager F. J. L. Blasingame, and C. Joseph Stetler, director of the A. M. A. Law Department. Those attending received first-issue copies of a new A. M. A. monthly news letter, *Citation*, which highlights the latest important court decisions or other legal developments affecting medicine.

SCIENCE FAIR WINNERS TO EXHIBIT IN SAN FRANCISCO

Two teen-age scientists, winners of the A. M. A. top honors at the National Science Fair in Flint, Mich., May 7-10, will be guest exhibitors of the Association at its Annual Meeting in San Francisco, June, 23-27.

For the third consecutive year, the A. M. A. participated in the fair by selecting four exhibits in the basic medical sciences. The two first place winners are Clare L. Chatland, aged 16, a junior in Missoula County High School, Missoula, Mont., and David R. Brown, aged 15, a St. Louis Park High School sophomore in Minneapolis. Clare's exhibit on "Hypersensitivity" shows the results of an experiment with the permeability of sensitized and nonsensitized membranes of mice. David's exhibit on "Humeral Transplants" shows how fetal mouse bones become ossified when transplanted into hostile mediums. Honorable mention citations were awarded to Barbara Ann Conway, aged 16, Chattanooga, Tenn., for her work with "Experimental Teratology," and to Robert LeRoy Sayre, aged 17, Huntington, W. Va., for his demonstration of "The Neurohumeral Theory and Cardiac Inhibition."

Congratulating the winners, Clare L. Chatland and David R. Brown, who will exhibit their work at the A. M. A. Annual Meeting in San Francisco, are, *left*, Dr. Otto J. Preston, chairman, National Science Fair executive committee, and, *right*, Dr. Thomas G. Hull, Chicago, Secretary, A. M. A. Council on Scientific Assembly, who served as a judge.

Dr. Alphonse McMahon, Chairman, A. M. A. Council on Scientific Assembly, and fellow Council members Drs. Stanley P. Reimann, Philadelphia, Henry R. Viets, Boston, and Thomas G. Hull, Chicago, chose the exhibits from a field of 281 entries from 41 states, the District of Columbia, Alaska, Hawaii, Germany, and Japan.

The awards were presented at an A. M. A. luncheon attended by 820 students, teachers, regional fair sponsors, press, and medical representatives. Dr. George W. Slagle, president, Michigan State Medical Society, presided over the presentations, and Dr. Otto J. Preston, chairman of the fair's executive committee and immediate past-president of the Genesee County Medical Society, Flint, announced the awards.

Many of the participating 146 regional fairs are co-sponsored and supported by local state and county medical societies, and the A. M. A. awards at the National Science Fair are the annual highlight of the medical profession's efforts to encourage talented students to undertake a medical career. The 1959 National Science Fair will be held May 6-9 in Hartford, Conn., and in Indianapolis, in 1960.

LETTER REGARDING FEDERAL CIVIL DEFENSE FUNCTIONS

May 13, 1958

Honorable Chet Holifield
Chairman, Military Operations Subcommittee
Committee on Government Operations
U. S. House of Representatives
Washington 25, D. C.

Dear Mr. Holifield:

The American Medical Association is advised that the President's Reorganization Plan No. 1 of 1958, providing new assignments for the conduct of federal defense mobilization and civil defense functions, is currently being considered by the Military Operations Subcommittee.

As the Association understands the proposed plan, its purpose is to enhance and make more effective the role of the Federal Government in nonmilitary defense programs. Under the Plan, the broad program responsibilities for coordinating and conducting the interrelated defense mobilization and civil defense functions would be vested in the President for appropriate delegation. The Office of Defense Mobilization and the Federal Civil Defense Administration would be consolidated in a new agency which would be known as the Office of Defense and Civilian Mobilization.

The basic concept of national mobilization is accepted as the "will of the people to resist." This concept depends on the sustained physical and mental health of the people and as such has interested the American Medical Association for many years.

In its concern with the health and medical aspects of civil defense, the Association has recognized, for a number of years, the urgent need for federal leadership, direction, and coordination. The Association believes that civil defense, like military defense, is an integral part of national defense which requires greater federal responsibility and leadership.

More specifically, the Association is concerned with the status, in any federal agency, of the office responsible for medical and health activities. The Association is convinced that medical and health activities are one of the most, if not the most, important function in sustaining the "will of the people to resist." In June, 1954, the Association's House of Delegates adopted a resolution requesting the Administrator of the Federal Civil Defense Administration to re-examine the position of the Health Division and to elevate that Division to a status commensurate with its obligations and responsibilities. In principle, this was ultimately accomplished in the December, 1957, reorganization of the Federal Civil Defense Administration with the creation of the position of Assistant Administrator, Health and Medical Affairs.

In June, 1956 the Association's House of Delegates approved the broad objective of strengthening the federal civil defense program, but was of the opinion that the method of accomplishing this was a matter for determination by the Congress with the advice and assistance of the President and the state governments.

In testimony before your subcommittee on March 7, 1957 on H. R. 2125, 85th Congress, the Association again emphasized that the medical and health functions of the civil defense program merit stature and prestige commensurate with the duties and responsibilities which must be assumed. Within the organization of the Office of Defense Mobilization there now is established a position of Assistant Director for Health and a civilian Health Resources Advisory Committee. The Association believes that the health and medical functions of the Federal Civil Defense Administration and the Office of Defense Mobilization must be maintained at top level in the organization of the proposed Office of Defense and Civilian Mobilization for the good of our country and our people should our nation ever again be confronted with another national emergency.

The Association is confident that the subcommittee, in furtherance of its serious efforts to strengthen the civil defense and mobilization program of our country, will give this matter of medical and health affairs the urgent and earnest attention which it merits.

We would appreciate it if you would make this letter a part of your official record of the hearings.

Sincerely yours,
F. J. L. Blasingame, M.D.
General Manager

TEACHING OF FORENSIC MEDICINE

The A. M. A. Committee on Medicolegal Problems, headed by Dr. Alan R. Moritz of Cleveland, is studying some suggested subjects in the field of forensic medicine for consideration and possible inclusion in medical school curriculums. Although the topic is integrated with other subjects in many medical schools, a number of schools now do not formally include forensic medicine in their instructional programs. Plans call for submitting an initial draft of the Committee's report to the Council on Medical Education and Hospitals for review and comment.

AMEF LISTS DIRECT ALUMNI SUPPORT TO MEDICAL SCHOOLS

A total of 50,364 alumni donated $3,020,600 directly to the 85 medical schools in the United States last year, according to a report of the American Medical Education Foundation, which handled an additional $984,884 in donations. Nearly half of the direct contributions, $1,467,098, were made without restriction, while the remainder were designated for building funds, research, student aid, rary, endowment, and other earmarked uses.

alifornia led the nation in total contributions, 2,883, through combined AMEF and alumni rts, and the state was also in first place in total s, 19,482—including a top-ranking number of 85 donations through the foundation. Direct peals brought $487,778 to California medical schools, more than to schools in any other state making such campaigns.

By individual school, the alumni of Jefferson Medical College in Pennsylvania led in number of direct contributors, 3,746. As the result of a special building fund campaign, alumni of the University of Vermont College of Medicine contributed the largest direct amount to a single medical school, $226,752. Other schools receiving large amounts in direct contributions through alumni drives (all more than $115,000) were Stanford University School of Medicine, University of Arkansas School of Medicine, College of Medical Evangelists, Harvard Medical School, Tulane University School of Medicine, New York University College of Medicine, Johns Hopkins University School of Medicine, and the University of Pennsylvania School of Medicine.

ACCREDITATION IN INDUSTRY

Representatives of the A. M. A. Council on Industrial Health and Council on Medical Education and Hospitals have joined with spokesmen for the Industrial Medical Association and the Joint Commission on Accreditation of Hospitals in discussions as to the possibility of developing a system for jointly accrediting occupational medicine services in industry. The first meeting was held in Chicago on May 15, and recommendations were sent soon afterwards to the respective parent-groups for action.

LIAISON WITH SCIENCE WRITERS

A cooperative effort to develop better liaison of the medical profession with newspaper science reporters has been launched by the A. M. A. and the National Association of Science Writers. The first of a series of regional workshops was held in Syracuse, N. Y., in April, for 70 participants from northeastern United States. Cincinnati was the scene of a second conference May 22. Present plans call for continuing the sessions—primarily panel discussions—in other parts of the country next fall.

Serving as co-chairmen of the Syracuse meeting were Dr. Robert J. Collins, president of the Onondaga County Medical Society, and Mrs. Cathy Covert of the Syracuse *Herald-Journal*. At a luncheon session, the first public report of Hungarian health under Communist rule was delivered by Dr. Lawrence H. Hinkle Jr., associate professor of clinical medicine at Cornell University Medical College. He said: "The Communists do not possess methods of persuasion, teaching or indoctrination that are superior to our own. This should go a long way toward dispelling the myth of so-called 'brain washing.'" Topics discussed at panel sessions included defining a good science story, a reporter's source file, how to use medical news sources, and ethics.

A similar pattern of panel discussions was used at the Cincinnati meeting. One highlight of that workshop was a report by Bernard C. Wexler, Ph.D., of Cincinnati on "Accelerated Aging in the Salmon and Its Application to Man." His study was made in collaboration with Dr. O. H. Robertson, emeritus professor of medicine at the University of Chicago School of Medicine. Dr. J. Robert Hudson of Cincinnati, and Don Dunham, science writer for the Cleveland *Press*, served as co-chairmen.

The National Association of Science Writers was founded in 1934. Its membership of 300 is confined to reporters who specialize in the writing of medical and science news.

HEALTH MESSAGES ON RADIO

The latest report of the Bureau of Health Education shows that 574 sets of A. M. A. transcriptions were in the hands of local broadcasters throughout the country as of April 28, 1958. Since there are 13 programs in each set, this represents about 7,500 local broadcasts which have been made, are being made, or will be made from these transcriptions. Some of the most popular series include "Menu for Health," 45 sets; "Harmony and Health," 46 sets; and "Interlude," 28 sets. Not included in these figures are the monthly platters entitled, "Health Magazine of the Air."

GRAND ROUNDS AT THE SAN FRANCISCO MEETING

The seventh in the series of Upjohn Grand Rounds telecasts will originate in San Francisco on June 25th, 1958 (6-7:30 p.m. Pacific daylight-saving time). This Grand Rounds will be the first of the series produced in cooperation with the American Medical Association and will be a part of the regular annual meeting. The program will be transmitted via closed circuit television to eight cities: Boston, Chicago, Cleveland, Kalamazoo, Mich., New York, Philadelphia, and Syracuse, N. Y. Physicians attending the meeting will have an opportunity to view the program in the War Memorial Opera House, one block from the Civic Auditorium.

The program will be in two segments. The first half-hour will be devoted to "Highlights of the Annual American Medical Association Meeting." Specially newsworthy scientific exhibits will be presented and the physician responsible for each of the exhibits will be interviewed. In addition, this segment of the program will present excerpts from some of the significant clinical papers that will be heard by those gathered in San Francisco. The second segment of the program will originate from the newly completed amphitheater of the University of California Medical Center. The subject to be discussed by a panel of outstanding physicians in the field of diabetes will be "The Current Therapy of Diabetes."

Case presentations of the patients from the wards and the outpatient clinics of the University of California School of Medicine will precipitate discussion of the recent developments in diabetes therapy, including the judicious utilization of the oral hypoglycemic therapy. The panel will also consider the question of shifting appropriate patients from insulin to oral tolbutamide therapy and delineate the proper steps and precautions in such a situation.

As usual, the entire program will be recorded on kinescope film and will subsequently be available for 16-mm. motion picture presentation to county medical societies and other professional medical groups.

CHANGE OF ADDRESS

If you change your address please notify The Journal at least six weeks before the change is made. Include the address label clipped from your latest copy of The Journal, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

COUNCIL ON MEDICAL SERVICE

CONFERENCE OF BLUE SHIELD PLANS

"Blue Shield's most significant problems lie in physician relations, national enrollment, federal legislation, and the development of more progressive forms of Blue Shield coverage."

Dr. A. J. Offerman, Omaha, retiring president, thus keynoted the 1958 Conference of Blue Shield Plans. The conference, held in Chicago the last week in April, was attended by approximately 700 persons.

In accepting Dr. Offerman's charge, the conference adopted a resolution in opposition to the Forand bill and revised its bylaws and membership standards. Other actions and discussions gave high priority to enrollment expansion, the effects of relative value studies on the plans, and the role of the physician in Blue Shield's future.

Dr. Carlton E. Wertz, Buffalo, was installed as President. Dr. Frank L. Feierabend, Kansas City, and Dr. M. Shelby Jared, Seattle, were named President-elect and Vice-president respectively. New officers of the Blue Shield Board of Directors (formerly Blue Shield Commission) include Dr. Donald Stubbs, Washington, D. C., Chairman; Dr. Henry Blake, Topeka, Vice-chairman, and Dr. Dwight Needham, Syracuse, N. Y., who was reelected as Secretary.

The conference's resolution opposing the Forand bill pointed out that of the 42 million Blue Shield subscribers "approximately 6.5% are in the age group of 65 years or over as compared with 8.5% of the total United States population 65 years and over."

Dr. Louis H. Bauer, Board Chairman of United Medical Service, Inc. of New York and Secretary-General of the World Medical Association, spoke on how plan trustees can best serve the future of Blue Shield.

In his address, Dr. Bauer said, "Some of our plans are no longer doctors' plans except in name. Not all of this is Blue Shield's fault, but often it is the fault of the medical society in letting control of the plan slip out of its hands. The fact remains, however, that, whatever the reason, it is the duty of the Board of Trustees to see to it that this control is strengthened or, where necessary, returned to where it belongs—in the hands of the profession. The key to the correct balance of Blue Shield strength lies in the relationship of the board to the medical societies it represents. . . .

"The medical societies should have the right to nominate the medical members of the Blue Shield Board. Ideally, in small plans, they can perhaps elect them. But no physician trustee should be elected unless he has been at least nominated or approved by the medical society of which he is a member.

"Plan trustees must see to it that no major change in policy is approved by the board unless the changes first meet with the approval of the medical societies. This applies to such plan policies as the extent of coverage offered, service benefit levels, fee schedules, and so forth."

Commenting on the relationship of Blue Shield to Blue Cross, Dr. Bauer said, "There was a tendency in the early years, because Blue Cross was the older, more experienced partner, for Blue Cross to become the dominant half of the liaison. Now, however, the situation is changed. Blue Shield has a depth of experience it lacked before and is growing faster than Blue Cross. I believe the two plans should now be partners on an equal footing. Neither should dominate the other.

"If we look at the plans around the country we see some of them completely divorced from one another. Others are almost completely unified, even to having the same personnel on both boards. Still other plans are separate except for a joint enrollment department. This, especially in the larger plans, has often proved a great convenience and saving to both plan and subscribers.

"Complete integration, even of just the boards, however, does not seem to me to be in the interest of anyone. Blue Cross is controlled by the hospitals and Blue Shield by the physicians—and their philosophies differ in so many respects that it is hard to imagine any joint board working smoothly without one plan overpowering the other.

"It is very disheartening to view the state of affairs that exists in those areas where the two organizations are more or less one in fact, even if not in theory. Because Blue Shield has been the junior partner it seems often to act hesitantly, without vigorous conviction in the course it must follow, content to be hand-led and spoon-fed by the elder Blue Cross. What is to be gained by one plan hiding in the shadow of the other? Blue Shield is no longer in swaddling clothes. It has reached adult state. Both plans are working to serve the community. They should work in harmony, yes—share those duties that will benefit both plans—but each plan should be master of its own fate.

"The first step that should be taken to establish a Blue Shield plan's independence is the appointing of a director separate from Blue Cross. Certainly, when Blue Shield was in its infancy, it could not afford a full-time director. Since there was need to establish a good deal of early planning, much was gained by having Blue Cross' director also serve Blue Shield. But, again, things have changed—and just as there is much to be gained by having separate boards, so is there much to be gained by each plan having its own director. The duties and responsibilities of each plan have grown to too great a height to allow one man to fulfill both jobs effectively without one being secondary to the other."

Dr. Offerman, in his presidential report, commented on the need for redoubling efforts to establish effective avenues of communication among all physicians and to create more opportunities for members of the profession to participate individually in the affairs of Blue Shield.

Also, Dr. Offerman said, "We must immediately devise better and more effective means of reaching the younger men entering the practice of medicine so that each new generation of physicians will be equipped to play a proper role in the development of our plans. The medical profession alone can provide the guidance and leadership essential to our progress. And this leadership can only be stimulated and assured if physicians understand the fundamental concept of physician sponsorship and guidance behind the growth and development of our community plans. For months—even years—we have told ourselves and agreed among ourselves that professional relations is the lifeblood of Blue Shield. It is time we demonstrate this tangibly with bold programs of action calculated to generate active physician participation in all the affairs of Blue Shield."

Elaborating on this theme, Dr. Ira C. Layton, Kansas City, in his address entitled "Charting a Course for Progress in Blue Shield," said, "I am convinced that the successful professional relations program can be carried out only by word of mouth from doctor to doctor.

"This necessitates a program of intensive training of a few physicians through the medium of board and committee activity so that facts may be carried to hospital coffee rooms and lounges, where they will be heard by other members of the profession. It necessitates our risking turnover of membership on our boards of trustees and on important committees, so that additional physicians may become better trained and better understand Blue Shield problems. Admittedly, this involves some risk; but without it, I fear we cannot succeed. In the broad sense, much can be done to improve professional relations by returning to the profession and to sponsoring medical societies the prerogatives of nomination and election of board members and by offering to the specialty societies the privilege of selecting members for important committees, such as fee schedule committees, arbitration committees, and others."

Both Dr. Offerman and the enrollment committee's report discussed progress in enrollment of national groups.

Dr. Offerman commented, "Out of the diversity of local Blue Shield programs traditionally aimed at meeting purely local needs and conditions, a pattern of benefits approaching the needs of national employers has been evolved. No one pretends that we have achieved the ultimate in our efforts to develop an entirely suitable national 'product.' It is, however, significant that we have made important strides in that direction. We have much more to do. Competition for enrollment among important national accounts is becoming more intense, and to meet it with success we will have to prepare Blue Shield to compete as favorably as possible for this business. Therefore, it is essential that we all contribute our best thinking in moving ahead toward a progressively better program of coverage for national employers. I would urge that this be an objective of first priority for each plan."

The enrollment committee reported that 39 plans agreed to underwrite the benefits of the national account agreement. These plans represent over 68% of the entire Blue Shield enrollment. A national group contract has been prepared, and Medical Indemnity of America, the central contracting agency, is now in the process of filing it with the New York State Department of Insurance. The committee emphasized the necessity for "a united front to the national market so that the name Blue Shield on a national contract will mean the same thing in all cases."

This committee also called for balanced benefits between Blue Cross and Blue Shield. In stressing the need for a policy of balanced benefits, this committee said, "A benefit structure weighted heavily in favor of either hospital or professional services invariably fosters dissatisfaction. This is reflected not only by initial buyer rejections of contract proposals, but by terminations of contracts due to dissatisfaction with the 'short' coverage in one area or the other. . . .

"We have recognized the often expressed opinion that the stubbornly limited benefits of Blue Shield upset the balance, and the converse opinion that Blue Cross "bids" a coverage which absorbs the bulk of the premium dollar. Both opinions may be valid in given references. . . . The buyer is concerned with the imbalance of benefits in the package, not with the circumstances which caused it . . . particularly when balanced coverages are available from sources other than Blue Cross and Blue Shield."

A discussion of relative value studies and their effects on Blue Shield plan operations produced one of the most interesting sessions of the conference. Drs. H. R. Pezzuti, W. H. Horton, C. D. Moll, and Nicholas F. Alfano, Medical Directors, respectively, of the Pennsylvania, Connecticut, Michigan, and New Jersey Blue Shield plans were the panel members.

Problems discussed included determination of appropriate relative values for nonsurgical procedures and the role of such studies in preventing the public's misunderstandings of fees.

Among the principles set forth in the membership standards adopted by the conference were the following:

1. A plan shall have approval of the state or county medical society, and, if the approving medical society withdraws its approval, such withdrawal shall place a plan's membership on a conditional basis, subject to termination, pending inquiry into the circumstances.

2. Subject to express provisions of law, there shall be free choice by the patient of any duly licensed physician practicing in the area served by the plan.

3. If a plan uses participating physician agreements which affect the benefits provided the subscribers, such plan shall maintain participation of not less than 51% of eligible doctors of medicine practicing in the area served by the plan.

4. The personal relationship between patient and physician shall not be abridged.

5. Benefits may be provided on an indemnity or service basis. Where indemnities are paid to the subscriber, it shall be clearly stated that they are for the purpose of assisting in paying the charges incurred for medical service and do not necessarily cover the entire cost.

6. A plan shall maintain an active program of professional relations directed toward maintaining close cooperation with practicing physicians. This program shall include annual reports of operations and progress to the governing body of the approving medical society, publication of a physicians' manual with all basic information pertinent to the plan's operation, maintenance of a committee or committees of doctors of medicine responsible for review of benefit schedules, review of medical claims requiring individual consideration, and establishment of claims administration policy.

MEDICAL NEWS

DISTRICT OF COLUMBIA

Abel Award to Dr. Mandel.—The American Society for Pharmacology and Experimental Therapeutics has presented the 12th annual Abel award to Harold G. Mandel, Ph.D., associate professor of pharmacology, George Washington University School of Medicine, Washington, D. C. The award, a $1,000 cash honorarium and a bronze medal donated by Eli Lilly and Company, Indianapolis, and sponsored by the society, is named in honor of the late John Jacob Abel, American pharmacologist and founder of the society. To be eligible for the award the candidate "must be under 36 years of age and must have exhibited unusual originality and independence of thought in the conduct of basic research in the field of pharmacology."

GEORGIA

A Medical Family.—Dr. Harold P. McDonald was named president-elect of the Fulton County (Atlanta) Medical Society recently, a few weeks after his brother, Pierce, was elected to the same office in the dental society. Harold is the son of Dr. Paul McDonald, 80-year-old general practitioner, and the father of two physicians, Lawrence and Harold Jr. Lawrence is now serving his internship at U. S. Naval Hospital, Bethesda, Md., and Harold Jr. is interning at Charity Hospital in New Orleans.

IDAHO

State Medical Meeting in Sun Valley.—The 66th annual session of the Idaho State Medical Association will be held July 6-9 at Sun Valley under the presidency of Dr. Hoyt B. Woolley, Idaho Falls. Each of the following guest speakers will present four papers in his specialty: Dr. Don H. O'Donoghue, professor of orthopedic surgery, University of Oklahoma School of Medicine, Oklahoma City; Dr. Horton C. Hinshaw, clinical professor of medicine, Stanford University School of Medicine, San Francisco; Dr. Carl A. Moyer, Bixby professor of surgery, Washington University School of Medicine, St. Louis; Dr. C. Donald Creevy, director, division of urology, University of Minnesota School of Medicine, Minneapolis; and Dr. Ralph C. Benson, professor of obstetrics-gynecology, University of Oregon School of Medicine, Portland. A golf tournament is planned, and facilities are available for tennis, fishing, and other sports. Entertainment includes the president's banquet July 9. For information write Mr. Armand L. Bird, Idaho State Medical Association, 364 Sonna Building, Boise, Idaho.

ILLINOIS

State Medical Election.—Dr. Joseph T. O'Neill, pediatrician of Ottawa, has been chosen president-elect of the Illinois State Medical Society, to assume the presidency in May, 1959, when he will succeed Dr. Raleigh C. Oldfield, of Oak Park, who has been installed as president. Other officers elected are: Dr. Lorne W. Mason, Evanston, first vice-president; Dr. Paul P. Youngberg, Moline, second vice-president; and Dr. Harold M. Camp, Monmouth, secretary-treasurer.

Chicago

Dr. Huggins to Receive Cancer Award.—Dr. Charles B. Huggins, professor of urology at the University of Chicago and director of its Ben May Laboratory for Cancer Research, has been named to receive the University of London's third Comfort Crookshank cancer research award, which will be conferred July 3 by Lord Astor of Hever, council chairman of the Middlesex Hospital of the College of Medicine at London in recognition of Dr. Huggins' "fundamental contributions to surgery of cancer." A lecture by Dr. Huggins will follow the presentation. The triennial Crookshank award consists of a silver medal and £250. It has been awarded only twice before, in 1951 to Prof. J. J. Bittner, of the University of Michigan, Ann Arbor, and in 1954 to W. Sampson Handley, of London. Dr. Huggins has been director of the Ben May Laboratory since 1951. On July 7, he will receive from the president of the German Federal Republic its Order "Pour le Merite."

Society News.—At the annual meeting of the Chicago Urological Society the following officers were elected: president, Dr. George O. Baumrucker, Hinsdale; vice-president, Dr. Cornelius W. Vermeulen; and secretary-treasurer, Dr. David Presman.——The Chicago Neurological Society has elected the following officers for 1958-1959: Dr. John J. Madden, president; Dr. Milton Tinsley, vice-president; and Dr. Meyer Brown, Evanston, secretary-treasurer.——At the annual meeting of the

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Metropolitan Dermatological Society of Chicago May 14 the following officers were elected: Dr. Henry H. Morrison, president; Dr. Boleslaw K. Lazarski, vice-president; and Dr. Tibor Benedek, secretary-treasurer.

LOUISIANA

Establish Chair in Epidemiology at Tulane.—A chair in epidemiology has been inaugurated at Tulane University of Louisiana School of Medicine by Mr. and Mrs. Charles E. Inbusch, of Milwaukee. The new chair will be known as the Dr. William Hamilton Watkins professorship in epidemiology and is named for the father of Mrs. Inbusch, the former Miss Dorothy Watkins of New Orleans. Dr. Watkins served as chairman of the Yellow Fever Board of New Orleans during the epidemic of 1897. He served as chief inspector of the New Orleans Board of Health and editor of the *New Orleans Medical and Surgical Journal.* He was one of the founders of the Louisiana State Medical Society in 1878 and served as president of the New Orleans Medical and Surgical Association in 1879.

Personal.—Dr. Henry C. Pitot, instructor in Pathology, Tulane University of Louisiana School of Medicine, New Orleans, has been awarded a Lillian Israel Memorial Postdoctoral Fellowship of the American Cancer Society. The fellowship will support the research and training of Dr. Pitot for three years. The grant will enable him to take a doctorate in chemical pathology and to continue research in protein synthesis in normal and cancer tissue under the direction of Dr. Emmanuel Farber, associate professor of pathology and biochemistry.

Society News.—At the annual business meeting of the Louisiana State Society of Anesthesiologists, the following officers were elected: president, Dr. Richard H. Morris, Alexandria; vice-president, Dr. John B. Parmley, New Orleans; and secretary-treasurer, Dr. William E. Trotti, New Orleans.

MAINE

Annual State Meeting in Rockland.—The 105th annual session of the Maine Medical Association will be held June 22-24 at the Samoset, Rockland. A discussion, "Health Insurance Is Here to Stay," June 23 will be followed by a question-and-answer period. The American College of Surgeons, Maine Chapter, will present "Environmental Sepsis" and "Streptococcus Infection in Practice." A panel discussion sponsored by the Maine Medico-Legal Society on the present status of the insanity plea in Maine in homicide cases will be moderated by Judge Charles A. Pomeroy, of Portland. Specialty groups will meet the morning and afternoon of June 24. Entertainment includes the golf tournament and the annual banquet, June 23, 6:30 p.m. For information write the Maine Medical Association, Dr. Daniel F. Hanley, Secretary, P.O. Box 240, Brunswick, Maine.

MASSACHUSETTS

Harvard Students Win Research Awards.—Allan Kliman, of Boston, a fourth-year student at the Harvard Medical School, has received the Soma Weiss award for 1958 for basic research carried on as an undergraduate at the school. His research concerned the mechanism of kidney damage following injection of bacterial extracts. Mr. Kliman's paper was one of seven selected for competition at the 18th annual Undergraduate Assembly of the Harvard Medical School, presented under the auspices of the Harvard Medical Society. Second award in the competition went to Robert Victor Moseley, a third-year student, for basic research in tissue transplantation; Elliot Vesell, a third-year student, received an honorable mention for research on enzyme activity in experimental shock.

Personal.—Dr. Sidney Farber, director of research at Children's Cancer Research Foundation, Boston, and professor of pathology, Harvard University Medical School at The Children's Hospital, has been appointed to serve on the National Advisory Health Council, the Surgeon General of the Public Health Service has announced.——Francis B. Carroll, area medical director of Veterans Administration hospitals and clinics for New England and New York, was given the annual Distinguished Service award by the Massachusetts Elks recently.——The annual Holmes Lecture of the New England Roentgen Ray Society was delivered by Dr. Patrick F. Butler, Boston, on "The Radiologist in Court," May 10.

MISSOURI

Personal.—Dr. Eric Reiss, assistant professor of medicine and preventive medicine and American Cancer Society scholar in medicine at Washington University School of Medicine, St. Louis, has been appointed director of the Irene Walter Johnson Institute of Rehabilitation currently under construction at the medical center. In his new position, Dr. Reiss will plan the program and arrange for the staffing of the institute. Activities of the institute, to be completed in the spring of 1959, will be coordinated through the department of preventive medicine and public health.——Dr. Charles J. Galbraith has been appointed senior instructor in surgery, Saint Louis University School of Medicine and chief of the Saint Louis University Surgical Service at Veterans Administration Hospital in St. Louis.

NEW YORK

State Medical Election.—Dr. Henry I. Fineberg, of Jamaica, was chosen president-elect of the Medical Society of the State of New York by the House of Delegates at the 152nd annual convention and will succeed Dr. Leo E. Gibson, of Syracuse, who was installed as president. Also elected were Dr. Harry Golembe, of Liberty, vice-president; Dr. Joseph A. Lane, of Rochester, speaker; and Dr. Frederick A. Wurzbach, Jr., of the Bronx, vice-speaker. The following were re-elected: Dr. Walter P. Anderton, of New York City, secretary; Dr. Ezra A. Wolff, of Forest Hills, assistant secretary; Dr. Maurice J. Dattelbaum, of Brooklyn, treasurer; and Dr. Samuel Z. Freedman, of New York City, assistant treasurer.

OREGON

University News.—Grants from the U. S. Public Health Service of $157,021 for research projects brought the total of grants received by the University of Oregon Medical School since the first of January to $475,385. Other gifts included $24,100 from the National Science Foundation for research in the division of neurology, $43,728 from the Atomic Energy Commission for research in experimental medicine and biochemistry, $15,000 from the Knights Templar Eye Foundation, $50,555.12 from the Medical Research Foundation of Oregon for studies in various Medical School departments; and $17,600 from the Life Insurance Medical Research Fund to further research on neurohumoral control of kidney functioning.

TEXAS

Workshop on Clinical Chemistry.—A Clinical Chemistry Workshop, sponsored by the Texas Section of the American Association of Clinical Chemists and Baylor University College of Medicine, Houston, will be held in the air-conditioned laboratory of the university's biochemistry department Aug. 18-22. The workshop will be designed to give the participants actual experience in carrying out some of the newer chemical methods useful in the clinical laboratory. The workshop will be open to qualified medical technologists, pathologists, and clinical chemists. Applications will be processed in the order received. Registration fee is $25 (make checks payable to Texas Section, AACC). For information write to the Division of Clinical Chemistry, Department of Biochemistry, Baylor University College of Medicine, Houston 25, Texas.

University News.—Mr. Leslie N. Pyrah, professor of urological surgery, University of Leeds, Leeds, England, presented "Urinary Diversion for Surgical Conditions" at the University of Texas Medical Branch, Galveston, Jan. 22.

WASHINGTON

University News.—Sir Howard W. Florey, 1945 Nobel prize winner, who was cited jointly with the late Sir Alexander Fleming for the discovery of penicillin and is now professor of pathology at the Sir William Dunn School of Pathology at Oxford, spoke at the University of Washington School of Medicine, Seattle, March 17 on the nature of the blood vessel lesion responsible for coronary artery disease.——A bachelor of science degree in physical therapy will now be awarded by the University of Washington, Seattle. The new curriculum will be offered under the department of physical medicine and rehabilitation in the School of Medicine, beginning next fall.

WISCONSIN

A Hobby Becomes a Company.—A hobby, fashioning images of human organs in plastic for tie clasps, cuff links, earrings and key chains, was started by Dr. Robert G. Zach, of Monroe, during World War II and has now developed into a substantial enterprise. He has organized a company which employs nine persons. Dr. Zach is a radiologist at the Monroe Clinic.

Annual Clinical Day.—The 11th annual clinical day of the Marquette University Medical School Dean's Committee will be June 21 at the Veterans Administration Hospital, Wood. The program will open with addresses by Drs. Charles P. Henke, director, professional services at the VA Hospital, and Edward A. Bachhuber, associate dean, Marquette University School of Medicine, Milwaukee. Moderators will be Drs. Joseph P. Looze and Raymond R. Watson. Thirteen papers are scheduled with the following authors: Drs. John J. Frederick (surgery), Reuben Beezy (medicine), Harry D. McGee, (otorhinolaryngology), George J. Owens (radiology), Richard O. Sternlieb (medicine), Jack D. Spankus (orthopedics), Albert M. Cohen (physical medicine), and William R. Taylor (medicine). For information write Dr. Jack J. Levin, Assistant Chief, Medical Service, Veterans Administration Center, Wood, Wis.

Institute of Art Therapy for Mental Patients.—Paintings and drawings created by mental patients in Wisconsin institutions were exhibited at the University of Wisconsin's first Institute of Art Therapy May 18-31, presented by the Wisconsin Psychiatric Institute. The 70 pieces were shown as tools for those who treat patients. Eight of Wisconsin's 37 state and county mental hospitals were represented, and there were pieces from the Northern and Southern Training Colonies for the Mentally Retarded, from the federal Veterans Administration Psychiatric Hospital at Tomah, and from the Jewish Vocational Service of Milwaukee, a private children's service. The patients ranged in age from 8 to 56. The institute is part of the new teaching program of the Psychiatric Institute, which was founded in 1915 under direction of the late Dr. William F. Lorenz, and became a university agency in 1925.

ALASKA

Dr. Gillett Named Deputy Health Commissioner.—Dr. James A. Gillett, who had been serving in the dual post of Fairbanks city health officer and northern regional health officer for the Alaska Department of Health since August, 1957, became Alaska's deputy commissioner of health, April 1. He came to Alaska last year from Australia, where he had been in private practice since 1951. A native of England, Dr. Gillett received his medical degree from the University of London Guy Hospital Medical School, a diploma in tropical medicine from the University of Edinburgh, and a master of public health from Johns Hopkins University in Baltimore.

GENERAL

Meeting on Vascular Surgery in San Francisco.—The 12th annual meeting of the Society for Vascular Surgery will be held June 22 at the Hotel Sir Francis Drake, San Francisco, with Dr. Frank L. A. Gerbode, president of the society, presiding. Seventeen papers are scheduled for presentation, including "The Rate of Healing of Arterial Autografs in Dogs" by Drs. Hyman Gaylis, and William P. Corvese, and Robert R. Linton. The presidential address, "Some Experiences With Intracardiac Surgery," will be presented by Dr. Gerbode at the luncheon. For information write the Society for Vascular Surgery, 4200 E. 9th Ave., Denver 20, Colo.

Establish Dr. Oughterson Memorial Fund.—The friends of the late Dr. Ashley W. Oughterson have established a memorial fund in the form of a trust "dedicated as a continuing memorial to Dr. Oughterson's work in the field of Medical Education, and to his assistance in the foundation of 'La Clinica de San Miguel Regla' in Mexico." The income from the fund will be used to furnish medical equipment and supplies serving about 4,000 medically indigent people of the Huasca Valley, Mexico. The clinic building, built and presented to the Mayor of Huasca in 1956 by the Club Panamericano de Doctores, has a staff of Mexican senior medical students assigned by their government to tours of duty of about six months. The establishment of the clinic was one of Dr. Oughterson's projects. Contributions may be sent to the Oughterson Memorial Fund in care of Dr. Arthur J. Geiger, 309 Edwards St., New Haven, Conn.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	May 24, 1958		May 25, 1957
	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	1
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	..	..	..
Middle Atlantic States			
New York	..	..	1
New Jersey	..	1	..
Pennsylvania	..	..	..
East North Central States			
Ohio	..	1	..
Indiana	..	..	..
Illinois	..	..	2
Michigan	..	..	1
Wisconsin	..	..	..
West North Central States			
Minnesota	..	..	..
Iowa	1	1	..
Missouri	..	..	3
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	..	4	4
Kansas	..	..	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	..	..	1
West Virginia	..	..	..
North Carolina	1	3	3
South Carolina	..	..	2
Georgia	..	..	1
Florida	1	2	1
East South Central States			
Kentucky	1	2	..
Tennessee	2	3	..
Alabama	..	..	2
Mississippi	..	..	..
West South Central States			
Arkansas	..	1	..
Louisiana	..	..	1
Oklahoma	..	..	..
Texas	5	9	18
Mountain States			
Montana	..	1	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	2
New Mexico	..	..	1
Arizona	..	..	..
Utah	..	1	4
Nevada	..	..	..
Pacific States			
Washington	..	..	..
Oregon	..	..	1
California	3	4	12
Territories and Possessions			
Alaska	..	..	..
Hawaii	1	1	..
Puerto Rico	2	2	..
Total	17	36	61

Annual Conference on Aging.—The University of Michigan, Ann Arbor, will present the 11th annual Conference on Aging June 23-25 at the Michigan Union in Ann Arbor. Four workshops are scheduled: (1) Social Gerontology as a Concept in Aging; (2) Individual Adjustments to Aging; (3) Impact of an Aging Society on the Individual; and (4) Applications of Social Gerontology to Social Action. A panel discussion, "Mobilizing Resources and Maximizing Opportunities," will be held the morning of June 25. Registration fee is $7.50. For information write the Department Extension Service, University of Michigan, 1610 Washtenaw, Ann Arbor, Mich.

Meeting of Catholic Hospital Association.—The 43rd annual convention of the Catholic Hospital Association will be held June 22-26 in Atlantic City, Four general meetings will emphasize the following topics: nursing as an important part of the apostolate, medico-social and economic changes, new concepts of management, and practical consideration of the health of the religious. Special meetings are planned on psychiatry, medical social service, emergency room, control of infection, disaster program, safeguarding newborn life, planning a poison control center, and geriatrics. For information write the Catholic Hospital Association, 1438 S. Grand, St. Louis 4.

Meeting in San Francisco on Angiology.—The fourth annual scientific meeting of the American College of Angiology will be held June 21-22 at the Fairmont Hotel, San Francisco. Two symposiums are planned: "Recent Advances in Cardiovascular Surgery" and "Experimental Angiology," moderated by Dr. Dwight E. Harken and George P. Fulton, Ph.D., respectively. Dr. Sidney S. Rose, consultant and surgeon, University of Manchester, England, will present "Treatment of Leg Ulcers" the afternoon of June 22. Round table discussions will be moderated by Drs. Harken, Rudolph Bircher, and John E. Estes. For information write Alfred Halpern, Ph.D., Secretary, American College of Angiology, 11 Hampton Court, Great Neck, N. Y.

Western Health Departments Win National Award.—The national Samuel J. Crumbine awards, a competition open to over 1,200 local health departments and sponsored by the Public Health Committee of the Paper Cup and Container Institute, New York City, were presented to the City of Spokane Health Department and the Los Angeles City Health Department on May 22 and 23. First place for "outstanding achievement in the development of a program of eating and drinking sanitation" was awarded to Spokane. Top honors for "outstanding achievement in the development of a comprehensive program of environmental sanitation" went to Los Angeles "with special consideration given to newly-developed activities of a pioneering nature which supplement its municipal program." Dr. Hampton H. Trayner, health officer, and Charles K. Reagan, chief general sanitarian of the Spokane Health Department, received personal medallions. Eight awards have been given since the start of the competition, established four years ago to honor Dr. Crumbine, pioneer American public health officer.

Lifetime Investigatorships.—The American Heart Association has announced the appointment of three "career investigators," bringing to six the number of scientists whose research is being supported on a lifetime basis by the association and its affiliates. The new career investigators are David B. Sprinson, Ph.D., professor of biochemistry, Columbia University College of Physicians and Surgeons, New York City; Dr. John V. Taggart, professor of medicine, also at Columbia; and Dr. Lewis W. Wannamaker, associate professor of pediatrics, University of Minnesota Medical School, Minneapolis. Already working as career investigators are Dr. Victor Lorber, University of Minnesota, appointed in 1951, and John R. Pappenheimer, Ph.D., and Dr. Albert H. Coons, both of Harvard Medical School, Boston, and both named in 1953. The career investigatorship is awarded to foster unrestricted research on a lifetime basis by outstanding scientists. Provided with $30,000 a year to cover the investigator's salary and underwrite the expenses of his laboratory, the recipient may work at any institution he selects and he is not obliged to report or publish except when he feels justified in doing so. Dr. Sprinson is working in the general field of intermediary metabolism. Dr. Taggart is a physiologist and biochemist whose chief sphere of interest is the kidney. Dr. Wannamaker's research is concerned primarily with the way in which streptococcal infections apparently "trigger" rheumatic fever. The awards are effective July 1. They bring to 186 the number of individual awards announced by the association and its affiliates for the forthcoming fiscal year, or a commitment of $1,523,000.

Medical Veterans Meeting in San Francisco.—The annual meeting of the National Medical Veterans Society will be held June 21-22 at the Hotel Sheraton-Palace, San Francisco. Dr. Milo A. Youel, president of the society, will address the group the afternoon of June 21. An informal forum June 22, 9.30 a.m., will include the following participants: Major Gen. Paul I. Robinson, (MC) U.S.

Army, director, Medicare; Mr. Thomas A. Hendricks, Field Director, A. M. A.; Dr. Russell B. Roth, Veterans Affairs Committee, A. M. A.; Major Gen. Silas B. Hays, Surgeon General, U.S. Army; Dr. Cyrus H. Maxwell Jr., acting manager, Washington Office, A. M. A.; Dr. Leroy E. Burney, Surgeon General, U.S. Public Health Service; and Rear Adm. B. W. Hogan, Surgeon General, U.S. Navy. For information write Dr. Henry C. Beekley, Secretary, 3117 Warsaw Ave., Cincinnati.

Applications for Heart Research.—Applications by research investigators for support of studies to be developed during the fiscal year beginning July 1, 1959, are being accepted by the American Heart Association. The deadline for Research Fellowship applications and Established Investigatorships is Sept. 15. Applications for grants-in-aid must be made by Nov. 1. Funds for association-supported research in the cardiovascular field are provided by public contributions to the Heart Fund. At least half of all funds received by the American Heart Association's National Office are allocated to research. Almost $31,500,000 has been allocated for research support by the association and its state and local affiliates and chapters in the past 10 years. Applications may be made for awards in the following categories:

Established Investigatorships: Awarded for periods of up to five years, subject to annual review, in amounts ranging from $6,500 to $8,500 yearly plus dependency allowance, "to scientists of proven ability who have developed in their research careers to the point where they are independent investigators." In addition, a grant of $500 is made to the investigator's department.

Advanced Research Fellowships: Awarded for periods of one or two years to postdoctoral applicants "who have had some research training and experience but who are not clearly qualified to conduct their own independent research." During the second year they will be permitted to spend up to 25% of their time in activities not strictly of a research nature, provided that these will contribute to their professional development and do not involve services for a fee. These stipends range from $4,600 to $6,500 annually. A grant of $500 is made to the investigator's department.

Research Fellowships: A limited number of awards is available to young men and women with doctoral degrees for periods of one or two years to enable them to train as investigators under experienced supervision. Annual stipends range from $3,800 to $5,700. This type of award is primarily made by local heart associations.

Grants-in-Aid: Made to experienced investigators to help underwrite the costs of specified projects.

Information may be obtained from the Assistant Medical Director for Research, American Heart Association, 44 East 23rd St., New York 10.

Report of Research Foundation.—In its annual statement for 1957, Research Corporation reported giving $1,257,000 in 364 grants last year, the largest dollar amount in its 46-year history. Since its foundation Research Corporation has granted a total of $12,757,000 for scientific basic research. Research Corporation is a nonprofit foundation established in 1912 by the late inventor-scientist Frederick Gardner Cottrell "to support research in the natural sciences in colleges, universities, and scientific institutions." The foundation receives its funds from its wholly-owned subsidiary, Research-Cottrell, Inc., manufacturer of industrial gas-cleaning equipment in Bound Brook, N. J., and from patents it administers for universities and individual inventors.

A Most-Wanted Fugitive.—Daniel William O'Connor, with aliases Clarence Baker, Daniel Baker, Bob Collins, James Garnie, Marcel Gelinas, Jacob Geres, H. A. Marceaux, Bill O'Brian, Jack O'Brien, Clarence William O'Connor, Bud Rogers, and others. Daniel William O'Connor is one of the FBI's Ten Most Wanted Fugitives. He is being sought for passing bad checks, and he is a deserter from the United States Army. He is also badly wanted by Canadian authorities on a charge of attempted murder in connection with an assault upon a Royal Canadian Mounted Police Officer. He has been known to travel with his wife, Mary Ursula, age 27, born Sept. 6, 1930, and their two sons, Danny William James O'Connor, age 7, born June 18, 1950, and Jack Kirkland O'Connor, age 6, born Nov. 17, 1951. O'Connor formerly was reported to have degenerative arthritis to a minor degree. His wife has an inguinal hernia on left groin and also has Rh-negative blood factor. Their son, Danny, reportedly has an ugly purplish red scar extending from hairline at center of forehead almost to his right eyebrow. It is requested that if any information comes to your attention concerning these individuals that the nearest office of the Federal

Most-wanted fugitive.

Bureau of Investigation be notified, telephone number of which can be found on the first page of the telephone directory. O'Connor is described as follows: Born Sept. 14, 1928, at Detroit; 5 ft. 7 in. to 5 ft. 9 in.; 200 to 260 lb.; blond hair; blue eyes; ruddy complexion; muscular build; noticeable dimple in chin. This man is known to be armed and considered to be extremely dangerous.

Society News.—The following officers of the **American Society for Surgery of the Hand** will serve for the current year: president, Dr. George V. Webster, Pasadena, Calif.; president-elect, Dr. Julian M. Bruner, Des Moines, Iowa; vice-president, Dr. Daniel C. Riordan, New Orleans; secretary-treasurer, Dr. George S. Phalen, Cleveland; and historian, Dr. Robert M. McCormack, Rochester, N. Y.——The **American Association of Genito-Urinary Surgeons** has elected the following officers: president, Dr. John A. Taylor, New York City; vice-president, Dr. Reed M. Nesbit, Ann Arbor, Mich.; secretary-treasurer, Dr. William J. Engel, Cleveland (reelected); and member of council, Dr. Carl F. Rusche, Los Angeles.——The following officers of the **Industrial Medical Association** have been installed: Dr. Hans W. Lawrence, Cincinnati, president; Dr. Dolor J. Lauer, Pittsburgh, president-elect; Dr. Robert E. Eckardt, Linden, N. J., first vice-president; Dr. John L. Norris, Rochester, N. Y., treasurer; and Dr. Leonard S. Arling, Minneapolis, secretary.——The **North Pacific Society of Neurology and Psychiatry** has elected the following officers: president, Dr. John W. Evans, Portland, Ore.; president-elect, Dr. Jesse L. Henderson, Seattle; secretary-treasurer, Dr. Robert M. Rankin, Seattle; and executive committee: Drs. Robert S. Dow, Portland, Peter O. Lehmann, Vancouver, British Columbia, Canada, and Wallace W. Lindahl, Seattle.——The **American Board of Surgery, Inc.**, has announced that after May 28 its office will be located at 1617 Pennsylvania Blvd., Philadelphia 3.

FOREIGN

Institute for Psychotherapy in Vienna.—An Institute for Psychotherapy has been initiated at the Psychiatric-Neurological Clinic of the University of Vienna, Dr. Hans Hoff, head, department of psychiatry and neurology, and chairman of the institute, announces: Purpose of the institute is "to give a comprehensive survey of modern psychotherapy and to impart theoretical and practical knowledge about all current approaches and techniques of psychotherapy." Various existing training possibilities will be supplemented as the institute will be conducted in close cooperation with university and clinic training facilities. The graduate of the institute is expected to have thorough theoretical and practical knowledge of all psychological treatment methods. The program will be for two years, i. e., four semesters. In the second year the methods of therapy of special groups of patients will be taught. Independent scientific research of the students will be encouraged. Qualified students from other fields can be admitted but are not permitted to take the examinations. For information write Dr. Hans Hoff, Director, Institute for Psychotherapy, Psychiatrisch-Neurologische, Universitatsklinik, Wien IX, Lazarettgasse 14, Austria.

Symposium on Carcinogenesis in London.—The Ciba Foundation will present a symposium, "Carcinogenesis: Mechanisms of Action," June 24-26. Eighteen papers are scheduled, including the following by U. S. participants:

Mechanisms of Carcinogenesis by Viruses, Dr. Jacob Furth, Boston.
Loss of Specific Cell Antigen in Relation to Carcinogenesis, E. C. W. Weiler, Pasadena, Calif.
Relation of Protein-Binding to Hydrocarbon Carcinogenesis, Charles Heidelberger, Ph.D., Madison, Wis.
The Nature of the Neoplastic Transformation in Lymphoid Tumor Induction, Dr. Henry S. Kaplan, San Francisco.
Studies on the Mechanism of Leukemogenesis by Ionizing Radiation, Dr. Arthur C. Upton, Oak Ridge, Tenn.

A reception at the Ciba Foundation will be held June 24 and a dinner, the evening of June 25, at which Professor Sir Macfarlane Burnet, F.R.S., will preside. The annual lecture for 1958 of the Society of Endocrinology will be given by Prof. O. Mühlbock at the Royal Society of Tropical Medicine and Hygiene, London, June 27 on "Hormonal Genesis of Mammary Cancer." For information write the Ciba Foundation, 41, Portland Place, London, W.I.

Turkish Center for Medical Training.—The Rockefeller Foundation has made a two-year grant of $170,000 to the Faculty of Medicine of the University of Ankara, Turkey which is enrolling increasing numbers of students from other Middle Eastern countries. Under a new arrangement, fees for the foreign group—about 25 out of each entering class—will be paid by the Turkish government. Until recently the medical curriculum at Ankara followed a traditional pattern. Two years ago the faculty inaugurated a system in the department of child health based on smaller classes and more laboratory and hospital experience, and then went on to incorporate similar changes in all the basic science and clinical departments. In the basic science courses students now spend two-thirds of their time in the laboratory and one-third in the lecture room. In their clinical years they divide into small groups for clinical and theoretical training and under a "clinical clerkship" requirement take medical histories, conduct physical examinations, assist at obstetrical deliveries, and perform other professional services under supervision. The foundation's grant will enable the faculty to purchase additional equipment and supplies outside Turkey. The Rockefeller Foundation in 1956 made a $100,000 grant to the university in support of its program in pediatrics.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: The American medical qualification examination to be given henceforth twice a year for foreign medical graduates. Medical Schools in the United States and Foreign Countries, Sept. 23. Final date for filing application is June 23. Executive Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Illinois.

BOARDS OF MEDICAL EXAMINERS

Arizona:* *Examination.* Phoenix, July 16-18. *Reciprocity.* Phoenix, July 19. Sec., Dr. Thomas N. Bate, 826 Security Bldg., Phoenix.

California: *Written Examination.* Los Angeles, August 18-21; Sacramento, Oct. 20-23. *Oral Examination.* San Francisco, June 14; Los Angeles, August 16; San Francisco, November 15. *Oral and Clinical Examination for Foreign Medical School Graduates.* San Francisco, June 15; Los Angeles, August 17; San Francisco, November 16. Sec., Dr. Louis E. Jones, 1020 N Street, Sacramento.

Connecticut:* *Examination.* Hartford, July 8-10. Sec., Dr. Creighton Barker, 160 St. Ronan St., New Haven.

Delaware: *Examination and Reciprocity.* Dover, July 8-10. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

Florida:* *Examination.* Miami, June 29-July 1. Sec., Dr. Homer L. Pearson, 901 N. W. 17th St., Miami.

Idaho: *Examination.* Boise, July 14-16. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Illinois: *Written Examination.* Chicago, July 7-11. *Oral Reciprocity Examination.* Chicago, July 11. Supt. of Regis., Mr. Frederic Selcke, Capitol Bldg., Springfield.

Maine: *Examination.* Augusta, July 8-10. *Reciprocity.* Augusta, July 8. Sec., Dr. Adam P. Leighton, 142 High St., Portland.

Massachusetts: *Examination.* Boston, July 15-18. Sec., Dr. Robert C. Cochrane, Room 37 State House, Boston.

Mississippi: *Examination.* Jackson, June 23-24. *Reciprocity.* Jackson, June 25. Asst. Sec., Dr. R. N. Whitfield, Old Capitol Bldg., Jackson 113.

Montana: *Examination and Reciprocity.* Helena, Oct. 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

New Hampshire: *Examination.* Concord, Sept. 10-13. *Reciprocity.* Concord, Sept. 10. Sec., Dr. Mary M. Atchison, Room 101, 61 South Spring St., Concord.

New York: *Examination.* Albany, Buffalo, New York City and Syracuse, June 24-26. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

North Carolina: *Reciprocity.* Blowing Rock, July 25. Asst. Sec., Mrs. Louise J. McNeill, Professional Bldg., Raleigh.

North Dakota: *Examination.* Grand Forks, July 9-11. *Reciprocity.* Grand Forks, July 12. Sec., Dr. C. J. Glaspel, Grafton.

Oregon:* *Examination.* Portland, July 16-17. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

Pennsylvania: *Examination.* Philadelphia and Pittsburgh, July 8-10. Acting Sec., Mrs. Marguerite G. Steiner, Box 911, Harrisburg.

Rhode Island:* *Examination.* Providence, June 26-27. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

South Carolina: *Examination.* Columbia, June 24-25. Sec., Dr. H. E. Jervey, 1329 Blanding St., Columbia.

South Dakota:* *Examination.* Rapid City, August 12-13. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Texas:* *Examination and Reciprocity.* Fort Worth, June 23-25. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Utah: *Examination.* Salt Lake City, July 9-11. Director, Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

Washington:* *Examination.* Seattle, July 14-16. Administrator, Mr. Thomas A. Carter, Capitol Bldg., Olympia.

West Virginia: *Examination and Reciprocity.* Charleston, July 14-16. Sec., Dr. N. H. Dyer, State Office Bldg., No. 5, Charleston.

Wisconsin:* *Examination.* Milwaukee, July 8-10. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., 1 West Wilson St., Madison.

Wyoming: *Examination and Reciprocity.* Cheyenne, Oct. 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

Alaska:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Guam: *Subject to Call.* Act. Sec., Dr. S. F. Provencher, Agana.

Hawaii: *Examination.* Honolulu, July 14-15. Sec., Dr. I. L. Tilden, 1029 Kapiolani St., Honolulu.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alaska: *Examination.* Juneau, Nov. 4. Sec., Dr. R. Harrison Leer, Room 204, Alaska Office Bldg., Juneau.

Arkansas: *Examination.* Little Rock, Oct. 6-7. Sec., Dr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.

Colorado: *Examination and Reciprocity.* Denver, Sept. 3-4. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Iowa: *Examination.* Des Moines, July 8. *Reciprocity.* Des Moines, July 7. Sec., Dr. Elmer W. Hertel, Waverly.

Michigan: *Examination.* Ann Arbor and Detroit, Oct. 10-11. Sec., Mrs. Anne Baker, 116 Stevens T. Mason Bldg., W. Michigan Ave., Lansing 15.

New Mexico: *Examination.* Santa Fe, July 20. *Reciprocity.* Santa Fe, June 26. Sec., Mrs. M. Cantrell, P. O. Box 1522, Santa Fe.

Oklahoma: *Examination and Reciprocity.* Oklahoma City, Sept. 26-27. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

Tennessee: *Examination.* Memphis, July 1-2. Sec., Dr. O. W. Hyman, 62 S. Dunlap St., Memphis.

Texas: *Examination.* October. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Wisconsin: *Examination.* Madison, Sept. 19. Sec., Mr. William H. Barber, 621 Ransom St., Ripon.

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*Basic Science Certificate required.

GOVERNMENT SERVICES

ARMY

Second Army Conference.—At the Second Army Civilian Medical Consultants' and Hospital Commanders' Conference at Fort George G. Meade, Md., May 28-29, called by Col. Francis P. Kintz, Second Army Surgeon, Dr. Manfred S. Guttmacher, chief medical officer, Medical Service of the Supreme Bench of Baltimore, talked on military psychiatry and criminology, and Dr. M. P. Hilleman, director of virus research, Merck, Sharpe & Dohme, talked on respiratory disease. Among the military guests were Major Gen. J. P. Cooney, Army deputy surgeon general, and Major Gen. I. S. Ravdin, retired, chairman, Second Army Civilian Consultants' Advisory Committee. The conferees included Second Army area hospital commanders with their chiefs of medical and surgical services, other representatives of the surgeon general's office, and civilian consultants assigned to headquarters, Second Army, and to Army hospitals in the Second Army area.

NAVY

Hospital Corpsman Selects Unknown Serviceman of World War II.—William R. Charette of Ludington, Mich., hospital corpsman first class, the only enlisted man on active duty in the Navy holding the Congressional Medal of Honor, was designated to select the World War II Unknown Serviceman to be committed to Arlington National Cemetery on Memorial Day, 1958. Charette, aboard the cruiser Canberra on May 26, in a ceremony off Norfolk, Va., made the selection from the remains of two unknown servicemen, previously selected in Epinal, France, and Honolulu who symbolize the Americans who died unidentified in European Operations and Pacific Operations during World War II.

The body of the Unknown Serviceman of the Korean war (selected in Honolulu on May 15), along with the World War II choice, was then transferred to Arlington National Cemetery for burial May 30, next to the Unknown Soldier of World War I. Both men lay in state in the Capitol Rotunda in Washington, D. C., before the Arlington ceremonies.

Charette, who is presently serving aboard the U. S. S. Quillback, was with the First Marine Division at the time he was cited during the Korean war for conspicuous gallantry. He was decorated by President Eisenhower at a White House ceremony on Jan. 12, 1954.

VETERANS ADMINISTRATION

Hospital Managers Transferred.—Transfer of five hospital managers has been announced.

Dr. Claud E. Carter, manager, VA Hospital, Butler, Pa., will become manager of the Fresno, Calif., VA Hospital, replacing Dr. Forrest G. Bell, who is retiring. Dr. Roland W. Hipsley, manager of the New Orleans VA Hospital, will be reassigned as manager of the Butler Hospital. Dr. Thomas L. Harvey, manager, VA Hospital, Montgomery, Ala., will become manager of the New Orleans Hospital.

Dr. Daniel H. Miller, manager, VA Hospital, Muskogee, Okla., will replace Dr. Harvey at Montgomery. To fill the vacancy at Muskogee, Dr. Alexander W. Kruger, manager, VA Hospital, Brooklyn, N. Y., will be transferred as manager. Dr. Henry L. Schmidt Jr., director, professional services, VA Manhattan Hospital in New York City, has been appointed manager of the Brooklyn Hospital.

PUBLIC HEALTH SERVICE

Dr. Lowry Appointed Assistant Surgeon General.—Dr. James V. Lowry has been appointed as chief of the Bureau of Medical Services with the rank of assistant surgeon general, succeeding Dr. John W. Cronin who died on March 26. The Bureau of Medical Services administers the Public Health Service hospitals, the Indian Health Service, Foreign Quarantine, the Hospital Survey and Construction Program, and research activities concerned with the nation's dental and nursing resources. Dr. Lowry, who entered the Public Health Service in 1937, is a diplomate of the American Board of Psychiatry and Neurology, and a past-president of the Kentucky Psychiatric Association.

Personal.—Dr. Arnold B. Kurlander has been appointed deputy chief of the Public Health Service Bureau of Medical Services. The bureau is responsible for administering Public Health Service hospitals, the Indian Health Service, Foreign Quarantine, the Hospital Survey and Construction Program, and research activities concerned with the nation's dental and nursing resources. He will succeed Dr. James V. Lowry, who has been named chief of the bureau. Dr. Kurlander has been a member of the Commissioned Corps since 1940.

DEATHS

Andrew, Richard M., New York City; New York Homeopathic Medical College and Hospital, New York City, 1891; died April 15, aged 97.

Armstrong, Arthur, Springfield, Mo.; Missouri Medical College, St. Louis, 1896; died April 5, aged 92, of senility.

Benz, Henry John, Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1904; an associate member of the American Medical Association; for many years chief of the city's school health service and superintendent of the bureau of child welfare; senior staff pediatrician, St. Joseph's Hospital, where he died April 4, aged 75, of bronchopneumonia, cerebral thrombosis, and gangrenous cholecystitis.

Blunck, Conrad Frederick Ernst, New York City; Columbia University College of Physicians and Surgeons, New York City, 1923; associated with St. Elizabeth's Hospital; died in Nyack (N. Y.) Hospital Feb. 2, aged 69, of coronary occlusion.

Box, William Lyles ⚕ Vernon, Ala.; Medical College of Alabama, Mobile, 1906; for many years county health officer; died April 1, aged 75, of cerebral hemorrhage.

Boyce, Samuel Robert ⚕ Gays Mills, Wis.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1899; fellow of the American College of Surgeons; died in Madison April 1, aged 95, of bronchopneumonia and cerebral vascular accidents.

Brake, John W., Cumberland Furnace, Tenn.; University of Tennessee Medical Department, Nashville, 1891; died in Clarksville April 1, aged 92, of a fractured hip.

Brittain, Oman R. ⚕ Salina, Kan.; John A. Creighton Medical College, Omaha, 1903; specialist certified by the American Board of Radiology; member of the American College of Radiology; veteran of World War I; on the staffs of St. John's and Asbury hospitals; died in St. Francis Hospital, Wichita, April 3, aged 79, of uremia.

Brown, Robert Dwight, East New Market, Md.; National Medical University, Chicago, 1897; an associate member of the American Medical Association; veteran of World War I; at one time associated with the U. S. Public Health Service Reserve and the Veterans Bureau; died March 31, aged 84.

Cusack, Thomas Stanislaus ⚕ Brooklyn; University and Bellevue Hospital Medical College, New York City, 1915; served on the staffs of Central Islip (N. Y.) State Hospital, Kings Park (N. Y.) State Hospital, and Samaritan Hospital; died April 14, aged 74.

Davison, Hal McCluney ⚕ Atlanta, Ga.; born in Woodville Oct. 2, 1891; Atlanta Medical College, 1915; for many years on the faculty of his alma mater, now Emory University School of Medicine; specialist certified by the American Board of Internal Medicine; past-president of the Southeastern Allergy Association, Medical Association of Georgia, American Therapeutic Society, and the Fulton County Medical Society; member of the American College of Allergists, of which he was past-president, and the American Academy of Allergy; fellow of the American College of Physicians; during World War I served with the U. S. Army, American Expeditionary Force in Siberia, where he worked with the American Red Cross the following year; trustee of the Mercer University, Macon; formerly on the staff of the Emory University Hospital, Grady Memorial Hospital, St. Joseph's Infirmary, and Crawford W. Long Hospital; for many years chief of medicine at the Georgia Baptist Hospital, where he died April 26, aged 66, of Hodgkin's disease and peritonitis.

Ellis, Leland Wadsworth, San Marino, Calif.; Stanford University School of Medicine, San Francisco, 1921; assistant professor of surgery at College of Medical Evangelists, Loma Linda and Los Angeles; an associate member of the American Medical Association; fellow of the American College of Surgeons; served on the staffs of the Alhambra (Calif.) Community Hospital, Garfield Hospital in Monterey Park, and St. Luke and Collis P. and Howard Huntington Memorial hospitals in Pasadena; died in San Gabriel April 10, aged 61, of coronary thrombosis.

Ensley, Bruce ⚕ Shell Rock, Iowa; State University of Iowa College of Medicine, Iowa City, 1907; died in the St. Joseph Mercy Hospital, Waverly, March 6, aged 79.

Estrin, Morris M. ⚕ Brooklyn; University of Colorado School of Medicine, Denver, 1923; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; served on the staffs of the Kings County and Adelphi hospitals; died in the Flower and Fifth Avenue Hospitals in New York City April 18, aged 58, of cancer.

⚕ Indicates Member of the American Medical Association.

Farrell, Martin Joseph, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1918; member of the medical staff at Misericordia Hospital, where he died April 8, aged 67, of cerebral thrombosis.

Fox, Denton Bernard, Grosse Pointe Park, Mich.; Loyola University School of Medicine, Chicago, 1937; died in the Jennings Memorial Hospital, Detroit, Feb. 3, aged 46, of cancer of the esophagus with metastasis to liver.

Furrer, Helen Hempstead, Cleveland Heights, Ohio; Johns Hopkins University School of Medicine, Baltimore, 1905; died Feb. 2, aged 78.

Gill, George, Elyria, Ohio; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1896; specialist certified by the American Board of Ophthalmology; fellow of the American College of Surgeons; associated with the Elyria Memorial Hospital, where he died April, aged 92, of cerebral thrombosis due to arteriosclerosis.

Green, Otto Ishmael ⊕ Bartlesville, Okla.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1912; on the staff of the Jane G. Phillips Memorial Hospital; died in Sand Springs April 4, aged 79, of lung cancer.

Hargreaves, Oliver Cromwell ⊕ Denver; Northwestern University Medical School, Chicago, 1904; veteran of World War I; died March 27, aged 85, of lobar pneumonia and cancer.

Harrigan, Thomas Joseph ⊕ Altoona, Pa.; Temple University School of Medicine, Philadelphia, 1937; member of the staff of the Mercy Hospital; died April 1, aged 46.

Harris, Clarence Newton, Indianapolis; Meharry Medical College, Nashville, Tenn., 1900; for many years city school physician; died April 6, aged 83, of cerebral thrombosis.

Heath, John Francis, Dayton, Ohio; Eclectic Medical College, Cincinnati, 1918; member of the Ohio State Medical Association; on the courtesy staff, Good Samaritan Hospital, where he died April 3, aged 71, of cerebral vascular accident.

Hendrick, Rhoda Grace, Tucson, Ariz.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1898; died April 3, aged 83, of bronchopneumonia, congestive heart failure, and arteriosclerotic heart disease.

Johannesson, Carl John ⊕ Portland, Ore.; born in Copenhagen, Denmark, March 29, 1891; Loyola University School of Medicine, Chicago, 1917; for many years practiced in Walla Walla, Wash., where he was past-president of the Walla Walla Valley Medical Society; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, Washington State Medical Association, and the Radiological Society of North America; veteran of World Wars I and II; for many years was associated with the Veterans Administration Hospital, Washington State Penitentiary, St. Mary's Hospital, and Walla Walla General Hospital, all in Walla Walla; died March 28, aged 66, of cancer.

Johnston, Florence Dorothy ⊕ Cedar Rapids, Iowa; University of Pennsylvania School of Medicine, Philadelphia, 1919; member of the American Society of Anesthesiologists; charter member of Iowa Anesthesiological Society; became librarian on July 1, 1923, of the American Medical Association and the following year assistant editor of THE JOURNAL, resigning in 1925 from this staff; associated with Mercy and St. Luke's Methodist Hospitals; died April 5, aged 65, of cerebral thrombosis.

Kaess, Andrew Joseph, Berkeley, Calif.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1903; veteran of World War I; at one time practiced in Moorhead, Minn., where he was coroner of Clay County, and at Fargo, N.D., where he was associated with St. John's Hospital; died April 11, aged 79.

Kampschmidt, August William ⊕ Bethlehem, Pa.; University of Missouri School of Medicine, Columbia, 1906; for many years practiced medicine in Columbia, Mo.; where he served as city health officer; member of the Missouri State Medical Association; died in St. Luke's Hospital April 7, aged 82.

Kelly, Harvey Augustine ⊕ Winthrop, Mass.; born in 1883; Baltimore Medical College, 1906; member of the American Academy of General Practice; past-president of the Massachusetts Academy of General Practice; past vice-president and for 20 years councilor of the Massachusetts Medical Society; past-president of the Suffolk District Medical Society; served on the hospital advisory board of the State Department of Public Health; veteran of World Wars I and II; served as medical director of the Winthrop public schools; one of the founders of Winthrop Community Hospital and served as its executive chairman for many years and president of its medical staff for five years; on the staff of the Chelsea (Mass.) Memorial Hospital; formerly staff member, Whidden Memorial Hospital in Everett; president of the Winthrop Cooperative Bank; member of the editorial board, *The New England Journal of Medicine;* died in the Phillips House, Massachusetts General Hospital April 8, aged 75, of pulmonary edema.

King, Ernest Harold, Tujunga, Calif.; Jefferson Medical College of Philadelphia, 1914; an associate member of the American Medical Association; veteran of World War I; died in Santa Monica March 24, aged 67.

King, Harry Clifton, Washington, D.C., Hahnemann Medical College and Hospital of Philadelphia, 1907; veteran of World War I; associated with the Hahnemann Hospital; died April 16, aged 73, of acute congestive heart disease.

Klaer, Clarence, Lock Haven, Pa., Hahnemann Medical College and Hospital of Philadelphia, 1896, an associate member of the American Medical Association; died in the Geisinger Memorial Hospital, Danville, April 11, aged 84, of cardiac failure.

Klostermann, George William ⊕ Irvington, Ill.; Homeopathic Medical College of Missouri. St. Louis, 1907; died April 7, aged 82, of coronary occlusion.

Knight, Robert Allen ⊕ Memphis, Tenn., born in Carter, Okla., Nov. 21, 1914; University of Oklahoma School of Medicine, Oklahoma City, 1938; assistant professor of orthopedic surgery at University of Tennessee College of Medicine; specialist certified by the American Board of Orthopaedic Surgery; member of the American Orthopaedic Association, American Academy of Orthopaedic Surgeons, and Clinical Orthopaedic Society; fellow of the American College of Surgeons; president of the American Academy of Cerebral Palsy, which he served as secretary-treasurer; associated with the Campbell Clinic Hospital, Hospital for Crippled Adults, Crippled Children's Hospital School, Baptist Memorial Hospital, Le Bonheur Children's Hospital, Methodist Hospital, St. Joseph Hospital, and U. S. Public Health Service Hospital; joint editor of the third edition of "Campbell's Operative Orthopedics"; died in Walnut Grove, Miss., April 13, aged 43, of injuries received in an automobile accident.

Leever, William Edward, Cincinnati; Medical College of Ohio, Cincinnati, 1901; died April 4, aged 83, of arteriosclerosis.

Levy, Albert Lewis, New York City; Cornell University Medical College, New York City, 1911; member of the Medical Society of the State of New York; specialist certified by the American Board of Orthopaedic Surgery; associated with the Hospital for Joint Diseases and Jewish Memorial Hospital, where he served as president of the medical board; died April 12, aged 68, of emphysema.

Lossow, Meyer Joseph, Alamo, Calif.; Cornell University Medical College, New York City, 1919; died March 28, aged 64.

Low, Victor, Honesdale, Pa.; Columbia University College of Physicians and Surgeons, New York City, 1899; served on the staff of the Farview State Hospital in Waymart; died March 18, aged 79. of heart disease.

Lucas, William Henry Sr. ⊕ Cedartown, Ga.; University of Louisville (Ky.) Medical Department, 1909; died in Atlanta March 25, aged 80.

Lull, Cabot ⊕ Birmingham, Ala.: University of Michigan Department of Medicine and Surgery, Ann Arbor, 1899; specialist certified by the American Board of Internal Medicine: past-president of the Jefferson County Medical Society; veteran of World War I; for many years medical director of the Anti-Tuberculosis Association of Jefferson County; associated with the Jefferson Tuberculosis Sanitorium, where he was past-president of the board and where, in 1953, the education building was named for him, South Highland Infirmary, and St. Vincent's Hospital; died March 31, aged 83.

McCarthy, Harriet Cecilia Schwartz ⊕ Kankakee, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1911; specialist certified by the American Board of Psychiatry and Neurology; associated with the Kankakee State Hospital, where she died March 25, aged 69, of coronary occlusion and hypertension.

Manion, Edward Bartholomew, Ilion, N.Y.; Albany (N.Y.) Medical College, 1910; for many years county coroner; served on the staff of the Ilion Hospital: died March 15, aged 70, of coronary embolism.

Martin, Zeno Thomas ⊕ Austin, Texas; University of Texas School of Medicine, Galveston, 1920; veteran of World War I; formerly city health officer; served on the staff of the Austin State Hospital; died March 28, aged 61.

O'Neal, Martha Margaret ⊕ Zanesville, Ohio; Western Reserve University School of Medicine, Cleveland, 1930; member of the American Academy of Pediatrics; past-president of the Muskingum County Medical Society; served as county health commissioner; associated with Good Samaritan and Bethesda hospitals; died in Cleveland Clinic Hospital March 28, aged 54, of aneurysm.

Orr, William H., Ventnor, N. J.; University of Louisville (Ky.) Medical Department, 1894; died Feb. 17, aged 88.

Papez, James Wenceslas ⊕ Columbus, Ohio; University of Minnesota College of Medicine and Surgery, Minneapolis, 1911; served on the faculty of Cornell University in Ithaca, N.Y.; at one time on the faculty of Emory University School of Medicine in Atlanta, Ga.; member of the Association for Research in Nervous and Mental Disease; director of the laboratory for biological research, Columbus State Hospital; died April 13, aged 74.

Pavlinac, Joseph Henry ⊕ Macomb, Ill.; George Washington University School of Medicine, Washington, D.C., 1925; died April 18, aged 57, of coronary thrombosis.

Pedersen, Victor Cox, Kensington, Md.; born in New York City Nov. 15, 1867; Columbia University College of Physicians and Surgeons, New York City, 1898; founder member of the American Board of Urology; in 1910 member of the House of Delegates of the American Medical Association; served as secretary and chairman of the genitourinary section of the New York Academy of Medicine; member of the American Urological Association and served as treasurer, vice-president, and president of the New York Society; member of the Society of Medical Jurisprudence, Society for Advancement of Clinical Research, Association of Military Surgeons of the United States, Military Order of Foreign Wars of the United States, and many other societies; fellow of the American College of Surgeons; an associate member of the American Medical Association; veteran of World War I; for many years practiced in New York City, where he was associated with St. Mark's Hospital; author of numerous books and articles on urology and sociology; died in the Le Deau Gardens Sanitarium in Forest Glen April 9, aged 90, of congestive heart disease.

Perrin, William, Rochester, N.Y.; New York Homeopathic Medical College and Hospital, New York City, 1901; associated with the Genesee Hospital, where he died April 7, aged 82, of nephrosclerosis.

Pope, Samuel Byron ⊕ Norfolk, Va.; Medical College of Virginia, Richmond, 1930; member of the American Academy of General Practice; on the staffs of the Norfolk General, Leigh Memorial, and DePaul hospitals; died April 2, aged 53, of a heart attack.

Preuss, Joseph George, New York City; Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau, Prussia, Germany, 1921; member of the Medical Society of the State of New York and the American College of Gastroenterology; on the staff of the Metropolitan Hospital; died March 30, aged 63, of coronary thrombosis.

Purcell, Ernest Francis Jr. ⊕ Trenton, N.J.; New York Medical College, Flower and Fifth Avenue Hospitals, New York City, 1947; certified by the National Board of Medical Examiners; member of the American Society of Anesthesiologists; veteran of the Korean War; associated with McKinley Memorial Hospital, where he died April 5, aged 36, of leukemia.

Read, Wilmot Deleo ⊕ Tacoma, Wash.; Cooper Medical College, San Francisco, 1903; fellow of the American College of Surgeons; past-president of the Pierce County Medical Society and the Washington State Medical Association; served overseas during World War I; first president of the Pierce County Medical Service Bureau and past-president of the Washington State Medical Bureau, which he helped found, predecessor of Washington Physicians Service; associated with the Tacoma General Hospital; died April 3, aged 78, of cerebral thrombosis.

Reils, Edwin August, Palmer, Neb.; University of Nebraska College of Medicine, Omaha, 1923; died in the Immanuel Hospital, Omaha, Feb. 16, aged 64, of cerebral hemorrhage.

Rice, Franklyn Augustus, Niles, Mich.; born in North Olmsted, Ohio, June 30, 1885; University of Wooster Medical Department, Cleveland, 1909; fellow of the American College of Surgeons; served overseas during World War I and later with the Army of Occupation; veteran of World War II and in 1946 was awarded the Legion of Merit for "his superior performance of duty as chief of the surgical service, Billings General Hospital, Fort Harrison, Ind., from March 25, 1943, to Dec. 3, 1945"; formerly practiced in Cleveland, where he was associated with the St. Vincent Charity and St. Luke's hospitals; associated with the Pawating Hospital; died April 9, aged 72, of lung cancer.

Root, Raymond Richmond ⊕ Georgetown, Mass.; Harvard Medical School, Boston, 1914; veteran of World War I; for many years school physician; on the staff of the Hale Hospital, Haverhill, where he died April 3, aged 76, of coronary occlusion and emphysema.

Ruhland, George Clemens ⊕ Washington, D.C.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1904; at one time on the faculty of his alma mater; veteran of World War I; served as commissioner of health of Milwaukee, Syracuse, N. Y., and the District of Columbia; formerly secretary-treasurer of the District of Columbia Commission on Licensure, and secretary of the Association of State and Territorial Health Officers; died in the Providence Hospital April 15, aged 79, of coronary heart disease.

Shnayerson, Edward Felix ⊕ Brooklyn; Cornell University Medical College, New York City, 1928; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the International College of Surgeons and the American College of Surgeons; veteran of World War II; associated with Coney Island and Maimonides hospitals, and the Caledonian Hospital, where he died April 10, aged 55.

Sloan, William Henry, Garland, N. C.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1916; member of the Medical Society of the State of North Carolina; veteran of World War I; on the staff of the Sampson County Memorial Hospital in Clinton; died in Durham April 9, aged 67, of heart disease.

Smith, Charles Enion ⊕ Chicago; Loyola University School of Medicine, Chicago, 1918; member of the American Academy of General Practice; on the staff of the Ravenswood Hospital; died April 21, aged 70, of cerebral hemorrhage, arteriosclerosis, and hypertension.

Smith, Harry Theopilus, Elverson, Pa.; George Washington University School of Medicine, Washington, D.C., 1904; past-president of the Chester County Medical Society; veteran of the Spanish-American War and World War I; served on the staff of the Pottstown (Pa.) Hospital; died in Pottstown April 15, aged 85, of uremia.

Snover, Clayton Halsey, Randolph, N.Y.; University of Buffalo School of Medicine, 1908; an associate member of the American Medical Association; served on the staffs of the Jamestown General Hospital and the Woman's Christian Association Hospital in Jamestown, where he died April 11, aged 75, of acute hemorrhagic pancreatitis.

Sullivan, Eugene Shaw, Madison, Wis.; Columbia University College of Physicians and Surgeons, New York City, 1918; fellow of the American College of Surgeons; on the staffs of the Madison General and St. Mary's hospitals; died April 8, aged 63.

Swan, James Hayes, Chambersburg, Pa.; Jefferson Medical College of Philadelphia, 1903; an associate member of the American Medical Association; past-president of the Franklin County Medical Society; associated with Chambersburg Hospital; died March 29, aged 85, of cerebral thrombosis.

Taylor, James Boyce, Huntington, W. Va.; Baltimore Medical College, 1894; in 1894 elected to the state legislature, and again in 1926 served as a state senator; formerly mayor of Huntington; served as president of the county board of health; formerly on the staff of the Chesapeake and Ohio Railway Hospital; died April 2, aged 89.

Thomas, Arthur W., Springfield, Mo.; University Medical College of Kansas City, Mo., 1895; died April 1, aged 86.

Thornburg, Maurice Redfield, Chicago; Northwestern University Medical School, Chicago, 1924; died in the Illinois Central Hospital April 6, aged 63.

Walker, Gale Havard ⊕ Polk, Pa.; University of Pittsburgh School of Medicine, 1930; member of the American Psychiatric Association; past-president of the Association of Mental Deficiency; formerly an officer in the regular Army; superintendent of the Polk State School; died April 22, aged 52, of acute coronary occlusion.

Wallerstein, Arthur Albert ⊕ Chicago, Ill.; Kaiser–Wilhelms–Universitat Medizinische Fakultät, Strassburg, Germany, 1902; veteran of World War I; on the staff of the Edgewater Hospital, where he died April 27, aged 79, of acute peritonitis with abscess and cancer of the gallbladder.

Weiss, Edward Hervey, Philadelphia; Jefferson Medical College of Philadelphia, 1927; member of the Medical Society of the State of Pennsylvania; associated with the Doctors and Misericordia hospitals; died in the Graduate Hospital of the University of Pennsylvania April 12, aged 54, of arteriosclerotic cardiovascular disease.

Wentz, Irl Zeigler ⊕ Seaside Heights, N.J.; Jefferson Medical College of Philadelphia, 1920; member of the American Academy of General Practice; school physician; died in Newport, N.C., April 5, aged 61, of a heart attack.

Wieters, John Christopher, Asheville, N. C.; Medical College of South Carolina, Charleston, 1912; member of the Medical Society of the State of North Carolina; died March 16, aged 67, of chronic myocarditis and arteriosclerosis.

Wilson, Robert Lee ⊕ Surgeon, U.S. Public Health Service, retired, Austin, Texas; University of Texas School of Medicine, Galveston, 1898; service member of the American Medical Association; retired from the U.S. Public Health Service in 1933; later employed as ship's doctor for several different steamship companies, principally the United Fruit Company; died April 1, aged 87.

Wittenberg, Harry J., Cincinnati; Cincinnati College of Medicine and Surgery, 1901; member of the Ohio State Medical Association and the American Trudeau Society; died April 4, aged 78.

Wood, Horatio C. Jr., Philadelphia; born in Philadelphia Feb. 26, 1874; University of Pennsylvania Department of Medicine, Philadelphia, 1896; emeritus professor of therapeutics at his alma mater and the University of Pennsylvania Graduate School of Medicine; emeritus professor of pharmacology at the Philadelphia College of Pharmacy and Science; chairman, Section on Pharmacology and Therapeutics, American Medical Association, 1906-1907; for many years member of the Committee of Revision of the United States Pharmacopoeia and served as vice-president of the United States Pharmacopoeial Convention; editor emeritus of "Dispensatory of the United States of America"; died March 31, aged 84, of cardiac failure.

Wright, Solon Westcott ⊕ Bessemer, Ala.; Birmingham Medical College, 1911; member of the American Acedemy of General Practice; veteran of World War I; died in Birmingham March 21, aged 73.

Wucher, Frederick Vaux ⊕ Pittsburgh; University of Pittsburgh School of Medicine, 1925; died in St. Francis General Hospital April 2, aged 60, of coronary thrombosis.

Zack, Arno Roy, Bethlehem, Pa.; Medico-Chirurgical College of Philadelphia, 1915; an associate member of the American Medical Association; on the staff of St. Luke's Hospital, where he died March 29, aged 67, of acute posterior myocardial infarction.

FOREIGN LETTERS

BRAZIL

Influenza and Antibiotics.—Dr. F. C. Algodoal (*Arquivos Médicos Municipais,* March, 1958) made no claim that antihistaminics prevent influenza, but they decrease susceptibility by eliminating an allergic component. Even if they do not inhibit the allergic component which facilitates infection, they may reduce congestion, edema, and coughing. Some antihistaminics also have a tranquilizing action and induce calm sleep. No known antibiotic is effective against influenza but penicillin V may be given by mouth to prevent secondary bacterial invasion.

Burns.—Dr. A. do Carmo Russo (*Revista Paulista de Medecina,* March, 1958) analyzed a series of 1,678 burned patients and found an increase in the incidence of burns from 0.32 per 1,000 in the period 1948 to 1951 to 0.62 per 1,000 in the period 1955-1956. The incidence of burns in children was 1.20 per 1,000 inhabitants, compared with 0.38 per 1,000 in adults. In this series 56.25% of the patients were under 15 years of age. Most of the patients (92.62%) were burned in or near home. In 64.2% the burns occurred in the kitchen. The incidence was greatest in the colder months and was greatest in housewives (50.38%). In 17.43% of the cases, more than one person was burned in the accident. Many burns were caused by explosion of alcohol ers or pressure cookers. Lesions caused by urning clothing occurred chiefly in girls. A great crease was noted in accidents caused by firecrackers.

CANADA

Supply of Physicians.—Dr. R. R. Struthers (*Canadian Medical Association Journal,* April 1, 1958) endeavored to show that Canada has an oversupply of medical schools, that several of these schools are hard pressed to recruit sufficient numbers of adequately prepared students, and that the present national population does not warrant 12 medical schools in terms of money for salaries of teachers and equipment or amount of teaching material. The population-physician ratio has remained constant in spite of the fact that almost 25% of the annual graduating class from Canadian medical schools eventually practice in the United States. Taking the average expectation of life for men 27 years of age, it may be assumed that the present number of 16,000 Canadian physicians will require replacement at about 3% per annum to compensate for deaths and retirements. Of the present 16,000, therefore, about 11,000 will still be in practice in 1965. If to this figure are added 800 graduates per annum for 10 years (the present graduation rate minus the loss to the United States) together with about 200 immigrants per annum, there will be a total of 10,000 added to the list, giving a grand total of 21,000 doctors in 1965. This number, on the basis of population forecasts, would be adequate.

Some valid objections may be made to these calculations. For example, the calculation should not be based on an average expectation of life at age 27, for it seems that at present there is a great hump in the physician population at around 45 years of age. This means that in 20 years there will be a mass retirement of physicians beyond the ordinary attrition. Moreover, no one can tell what demands will be made on the profession by the introduction of hospital insurance, possibly supplemented by further insurance benefits to the general population. The deans of medical schools, however, are worried not about the quantity but about the quality of applicants to their schools.

Hospital Insurance.—The federal government has got the requisite six provinces to participate in the Federal-Provincial Universal Hospital Insurance Scheme. Of the remaining four all but Quebec are also falling into line. Manitoba is the latest to announce its plans, and although they have been slow in appearing, the start of this scheme is being hastened, and it should become effective in July. The scheme does not differ greatly from that announced by Ontario. It provides standard (public) ward accommodation with no time limit; necessary nursing services; laboratory, roentgenographic, and other diagnostic services; drugs, biologicals, and related preparations; use of operating room; anesthetic facilities; routine surgical supplies; radiotherapy; and physiotherapy. Like Ontario's scheme, it covers emergency services for injured persons on an outpatient basis within 24 hours of an accident. Manitoba has managed to shave 5 cents a month off the Ontario cost, for the basic cost in premiums will be $2.05 for an individual and $4.10 for a family. The government will carry the cost for the first six months, the premiums starting on Jan. 1, 1959. Social security cases will be covered free. Mental and tuberculous patients are also given full hospital coverage, although the federal government does not include this service in its plan. Costs of this additional service will be borne by the province. There will be no deterrent charges, deductible

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The items in these letters are contributed by regular correspondents in the various foreign countries.

clauses, restrictions against age, or time limits. Firms employing five or more persons will register their employees and collect the premiums. Self-employed and other persons will register at municipal offices. Any person laid off work and having his premiums paid up to date will have his hospital insurance continue in force for at least six months after his layoff. The scheme is compulsory, and anyone who fails to join may be fined up to $200.

Medical Bacteriology.—The medical bacteriologists of Canada are worried about their current status. The recruitment of young medical graduates into this specialty has been poor of late. The broad field of bacteriology, including virology, mycology, and parasitology, is inadequately covered by the 78 medically qualified bacteriologists of Canada, even with recruitment from Europe. There is no doubt that further demands will be made on the specialty when the hospital insurance scheme begins. Lack of adequate recruitment is blamed on the poor economic returns, the lack of established positions in the larger hospitals and health departments, and the lack of adequate training grants. The Canadian Association of Medical Bacteriologists believes that many jobs can be done only by medically qualified bacteriologists, but that if recruitment continues to be poor they will have to be filled by persons without proper qualifications. They recommend that each teaching hospital in Canada accredited for advanced graduate training in medicine or surgery and each large general hospital should have on its staff a medically qualified bacteriologist on a full-time basis. They recommend that such bacteriologists should enjoy the same income as other medical laboratory specialists and that adequate training grants should be established to allow attendance at formal university courses leading to a higher qualification in bacteriology.

DENMARK

Tuberculosis Morbidity.—Dr. E. Groth-Petersen (*Ugesk. læger,* March 20, 1958) compared the tuberculosis morbidity among persons over 15 who were tuberculin-positive with the morbidity among adults in the population as a whole in the period 1952 to 1955 inclusive. The tuberculosis morbidity per 100,000 in the first group fell from 44 to 36, whereas in the latter it fell from 41 to 21. The difference in favor of the latter was greatest in respect of young adults. The first group, it should be noted, were tuberculin-positive as a result of infection and not to BCG vaccination. Groth-Petersen concluded that fully one half of the adult population of Denmark is still tuberculin-positive as a result of infection.

Cerebral Abscess.—Dr. C. V. Fog (*Nord. med.,* April 3, 1958) studied a series of 114 patients with cerebral abscess and found that 33 were otogenic, 6 were rhinogenic, 28 were thoracogenic, 11 were craniotraumatic, and the remaining 36 were of some other origin. Supratentorial greatly outnumbered infratentorial abscesses. Those of thoracic origin were so severe that 21 of the 28 patients died. A classification hinging on the bacteriological findings showed that 11 of the 23 patients in whom Staphylococcus pyogenes var. aureus was found died, whereas there were only 6 deaths among the 24 for whom culture proved sterile. Of the 17 in whom streptococci were found 12 died. There were 65 deaths in all. Even with the use of an antibiotic a 25% mortality must be expected. A follow-up examination of the 49 survivors revealed that 31 were fit for work. Of the 18 remaining 13 had become epileptic. Total excision did not seem to give a higher mortality than more conservative measures.

Staphylococcic Infections in Hospital.—At a meeting of the Danish Society for Internal Medicine, reported in *Nordisk medicin* for April 17, several speakers stated that staphylococcic infections were a serious hazard on medical as well as surgical wards. On the medical side of the Blegdam Hospital between March, 1954, and the end of 1956 there were 55 such cases, the infection having been brought in from the outside in 14 cases and being nosocomial in 41. Of the 5 that were very serious, 3 were enteritic, and these patients successfully responded to erythromycin. The phage-type 80 organisms responsible for infections in Australia at the same time, gave rise to an outbreak of boils and abscesses in seven patients and one nurse in a 16-bed ward. Nearly all the victims of this type were elderly and debilitated women. The present high rate of staphylococcic infections may largely be due to a change in the composition of hospital patients who now are often old, debilitated, and just kept alive by modern methods of treatment. Systematic bacteriological examinations of the nurses in 8 surgical hospital units in Copenhagen showed that over 50% harbored Staphylococcus pyogenes var. aureus in the nose and that 86% of these were penicillin-resistant. About 67% of these nurses lost their staphylococci when on vacation. Another speaker remarked on the curious immunity to infections of the nose with staphylococci enjoyed by some nurses. His remedy for staphylococcic hospital infections was to discontinue the indiscriminate prophylactic use of antibiotics on a grand scale. He referred especially to an epidemic of measles in which 30% of the recipients of prophylactic treatment with penicillin developed secondary infections, whereas this was the case with only 15% of the patients not so treated. He also referred to the likelihood of the recipients of prolonged treatment with steroids to develop staphylococcic infections.

INDIA

Pathogenicity of Entamoeba Coli.—Kasliwal and Sogani (*Indian Journal of Medical Sciences*, vol. 12, February, 1958) stated that although it was first thought that of the intestinal protozoa only Entamoeba histolytica was pathogenic, doubts have been raised from time to time and evidence is now available to show that E. coli is capable of ingesting red blood cells both in culture and in the intestine. The authors observed 43 patients with colitis in whom no evidence of E. histolytica infection was found on repeated stool examination. The age of these patients varied between 8 and 70. They complained of abdominal pain, anorexia, diarrhea or constipation, and vomiting. The liver was palpable in 32. One had an amebic abscess from which 13 oz. of typical pus was aspirated. Microscopic examination of the pus showed Charcot-Leyden crystals, fatty acid crystals, and degenerated liver cells, but no protozoal growth was obtained on culture and no other organisms could be grown. The cecum was palpable and tender in 12 patients and the descending colon in 27.

Stools of all the patients showed E. coli infection. Other parasites associated with it were Giardia lamblia in four, Iodamoeba buetschlii in four, and Ankylostoma duodenale in one. Stool cultures were made from 25, and of these 15 showed pure E. coli growth. Sigmoidoscopy was performed on 14, of whom 10 showed a normal mucosa. One to three small ulcers with raised margins were seen in the rectosigmoid of the other four. Microscopic examination of scrapings from these ulcers showed trophozoites of E. coli in two. Most patients had mild to moderate anemia. Of the 43 patients, 9 left against medical advice and the rest received emetin followed by carbarsone or iodochlorhydroxyquin after a preliminary treatment with penicillin to overcome the secondary infection; 17 obtained complete relief and the rest had a varying degree of symptomatic relief. At the time of discharge only 8 of the 34 were passing cysts of E. coli in their stools. The colon was not tender in any patient after treatment. Before treatment, 15 of the 34 had an enlarged tender liver, but after treatment the liver was barely palpable and slightly tender in only 2 and palpable but not tender in 2. These patients thus showed the clinical findings of amebiasis and were greatly improved after antiamebic treatment, but repeated stool examinations were negative for E. histolytica while E. coli was found in all and also in scrapings from intestinal ulcers. This was considered strong circumstantial evidence that the latter is a pathogen.

Tuberculosis in the Army.—Pulmonary tuberculosis is the principal cause of separation from the Army, with injuries and psychiatric diseases following in second and third place. M. C. Sanyal (*Indian Journal of Tuberculosis*, vol. 4) collected data over a two-year period from hospitals where patients with pulmonary tuberculosis were admitted; from the annual health reports of the Chief Sanitary Commissioners, the Public Health Commissioners, and the Army; and from the results of mass miniature radiography in military hospitals—the records of 9,278 persons in all. Since 1900, the incidence of pulmonary tuberculosis in the Army declined from 3.7 per 1,000 in 1900 to 1.24 per 1,000 in 1949. The incidence was never high during this period although there were peaks coinciding with World Wars I and II. The fall was steady and slow and was more likely the result of a social trend than of any preventive measures. A study of age incidence showed a small rise up to the age group 40 to 45 years, then a slight fall, and the final rate was a little higher than in the age group of 18 to 20 years.

In Gurkhas and hill people there was a definite peak in the age group 30 to 35 years. This is to be expected in a population with relatively little contact with pulmonary tuberculosis and therefore little immunity to it. Meeting the disease for the first time in adolescence and early adult life, they have a much higher incidence than other adults in the Army who have been in contact with it since childhood. In the age group 18 to 20 years, the training period of recruits, there was no pulmonary tuberculosis among Gurkhas. Results of mass miniature radiography showed that among the naval personnel examined, of the total detected abnormalities, pulmonary tuberculosis comprised 52.9%. This incidence was 81.4% in trained Gurkha soldiers and 30.7% among untrained Gurkhas. The artillery and infantry (the two branches which involve heavy physical stress and strain) and Army medical personnel whose duties involve caring for tuberculous patients showed the highest incidence of this disease. A much higher incidence was observed among the married than among the unmarried men. The campaign against pulmonary tuberculosis at present provides mass miniature radiography of Gurkha recruits before acceptance and BCG vaccination of all susceptibles among Gurkhas. This is also extended to their family members. A follow-up of family contacts in a household where one member is suffering from this disease is also advised.

Effect of Hypothermia on Brain and Heart.—B. K. Anand and co-workers (*Indian Journal Medical Research*, vol. 46, January, 1958) stated that although hypothermia has offered new prospects in the treatment of congenital heart disease, cerebral vascular tumors, and aneurysms, its use is attended by certain hazards. It induces serious cardiac arrhythmias and irreversible changes in the nervous system, especially in the heart regulating mechanism and the respiratory and cardiovascular centers. These complications have been variously assigned to conflicting mechanisms. The authors estimated the acetylcholine and glutathione content of the heart and brains of 6 normal and 14 hypothermic dogs. The normal averages of acetylcholine and glutathione content of the heart, hypothalamus, and frontal and temporal lobes of the brain were worked out from the values obtained in the control animals. The acetylcholine level of the heart was lower than that of the nervous tissue and the hypothalamic region contained an appreciably higher level than the frontal and temporal lobes. The glutathione content of the heart was also lower than that of the nervous tissue but the hypothalamus contained about the same amount as the frontal and temporal lobes.

An average fall of 14.5 C below the average body temperature was obtained by hypothermia. Hypothermia of this degree decreased the amounts of both acetylcholine and glutathione in the heart and the hypothalamic and frontal regions of the brain, but it increased both the acetylcholine and glutathione content of the temporal lobes containing the hippocampus. As the periamygdaloid region containing the hippocampus is related to the maintenance of body temperature, this region may be becoming hyperactive to counteract the hypothermia and maintain the normal surface and visceral temperature. The increase in the acetylcholine and glutathione is a result of the increased metabolic activity. In the heart and nervous tissue, the cellular metabolism is diminished during hypothermia and this is reflected in the loss of the two chemicals studied here. The authors suggested that it may be profitable to give adequate doses of acetylcholine and glutathione during hypothermia to prevent abnormal rhythms in the heart and failure of the vital nervous centers. This is especially important in the recovery phase when the temperature starts rising, as at this time metabolism in the tissues is increased and there is likelihood of the development of anoxemia.

NEW ZEALAND

X-ray Hazards.—The New Zealand branch of the College of Radiologists of Australasia in a report on radiation dangers stated that the risk of danger from a diagnostic x-ray examination by a properly trained operator is nonexistent, but it warns that too many reexaminations in any anatomical site are at present being undertaken without critical appraisal of the need for such examination. Much unnecessary apprehension has been created by public statements of the risks, not counterbalanced by any consideration of the value, of medical x-rays. There is some ground for supposing that unborn children are more sensitive to x-rays than adults, but so far exhaustive research has not proved that x-ray examination of the mother involves a significant risk for the child. Against this possibility must be balanced the certain risk to mother and child if x-ray examination is omitted when it would have been helpful. In diagnostic x-ray examination by a skilled operator the dose is so small that the risk of any genetic effect is remote. By continued improvement of the already very safe conditions under which x-ray examinations are made scientists are reducing such risks to an even lower level, and, in some cases, eliminating them completely. The college believes, however, that routine roentgenography of the chest in persons under 16 years of age is not justified. Reexamination of patients with known tuberculosis should be preceded by a clinical examination to determine, among other things, the necessity for roentgenographic reexamination. Any program, such as national mass surveys, and routine examination of specific groups, such as nurses, should be the subject of periodic review to determine whether continuance or modification is justified by the results being obtained.

Endocrine Homotransplants.—Woodruff and Sparrow who previously showed that rats injected subcutaneously with homologous spleen cells in suitable dosage on the day they are born are, when they grow up, almost completely tolerant of skin homografts from the same donor, now report the results of some experiments designed to determine whether tolerance induced in this way might be extended to homografts of other tissues, especially of thyroid and adrenal tissues (*Quart. J. Exper. Physiol.* 43:91, 1958). Litters of newborn Wistar rats were subdivided into four pairs of animals of like sex. One member of each pair received a subcutaneous injection of a suspension of spleen cells from an adult of the same sex, and the other member served as a control. When they were 12 weeks old, each injected animal received a homograft of either thyroid or adrenal tissue from the original cell donor and each control animal a homograft of thyroid or adrenal from a stock rat of the same sex.

The technique for assessing the viability of thyroidal grafts consisted of measuring the uptake and release of I ^{131} from the thyroid grafts. These measurements provided a useful means of assessing the amount of surviving thyroid tissue and its functional activity. Homografts of thyroid tissue placed alongside the femoral vessels in thyroidectomized rats, injected at birth with spleen cells from the same donor, were as a rule indistinguishable from autografts both in their capacity to take up I ^{131} and in their histological structure, whereas homografts in thyroidectomized but otherwise untreated rats were usually destroyed within six weeks. Homografts of whole adrenal glands sutured to the ovaries of adrenalectomized recipients which were injected at birth with donor spleen cells also behaved like autografts. Homotransplants in adrenalectomized control hosts were sometimes destroyed in a few weeks, but sometimes survived for months, though they usually showed evidence sooner or later of replacement of cortical tissue by connective tissue.

the arms and legs led to the drug being withheld. With a smaller dosage (1 mg. daily, raised in 2 to 3 weeks to 5 mg. daily) encouraging results were obtained. All the patients noted a lessening of rigidity and most of them less tremor. The gait became more natural and the facial expression more relaxed. In most patients sleep was improved. Several patients noticed slight dryness of the mouth, and two had slight blurring of vision. With the exception of the victim of overdosage, all the patients were anxious to continue this treatment, which was, however, hampered by its high cost.

Cancer from Medicinal Use of Arsenic.—Dambolt and Foss (*Tidsskrift for den Norske lægeforening*, April 1, 1958) condemned the vogue for prescribing arsenic for a great variety of ailments. They have treated four patients whose cancer followed the prolonged administration of arsenic. The lungs were invaded in two of these, and keratoses due to arsenic were observed in three other patients after prolonged arsenic medication. The authors sent a questionnaire to 90 patients who had survived an operation for lung cancer. Of the 74 who answered 12 had had a course of arsenic treatment much earlier in life. To learn the extent to which such courses are popular, 248 skin patients over the age of 20 were asked if they had ever had such a course, and it was found that 19% had. In the last 27 years an average of 50 kg. of arsenic have been sold yearly by druggists in Norway. These sales have declined somewhat in recent years. The authors challenge the basis on which arsenic has been prescribed since cases of carcinoma due to arsenic were first reported in 1887. Arsenic may have fallen into disrepute as a general tonic and as a treatment for acne, eczema, and alopecia, but opinions are still divided over its value in treating psoriasis. Although its use is still justifiable in some cases caution is needed if the complaint is chronic and particularly if the patient is young. In treating pityriasis rubra pilaris arsenic may be beneficial and even indispensable if the patient is middle-aged or elderly. The same may be said of Boeck's sarcoid, but in general arsenic should be prescribed with great parsimony and circumspection.

Sedimentation Rate and Serum Cholesterol.—At the Kroghstötten hospital in Oslo, several patients were found to have a high sedimentation rate of unknown origin associated with a pathologically high total serum cholesterol concentration. Dr. Jarle Ofstad (*Nord. med.*, April 17, 1958) reviewed the records of 19 patients with primary hypercholesterolemic xanthomatosis with special reference to their sedimentation rates and found that the rate rose with the rise of the concentrations of total cholesterol, free cholesterol, phospholipid and, in some degree, beta-globulin. Although his series was too small to warrant any conclusion as to a causal relationship, they make such a relationship appear likely.

Blood Pressure.—The late Professor H. Rasmussen devised an ambitious plan for an investigation of the blood pressure of the inhabitants of Bergen, in connection with a more or less compulsory mass roentgenography survey of its population in 1950-1951. The ages, heights, and weights of the subjects were also recorded. Fröystein Wedervang analyzed this series of about 70,000 observations for his doctor's thesis. He concluded that the blood pressure rises with age, being lower among young females than males of the same age but the rise with growing years is greater for females than for males till they run level, and ultimately the pressure is higher in the female. Within each age group there are wide variations in the range of pressure measurements, and this range grows with age. It is commonly assumed that overweight sends the blood pressure up, but if it does so, the figures are not impressive, with a rise of only 2 or 3 mm. Hg for every 10 kg. of body weight gained. The height-weight measurements showed among other things that, with a given height, there was a marked mean rise of weight with increasing years, overweight being conspicuous for women between the ages of 45 and 65.

SWITZERLAND

Psychomotor Aspects in Children with Behavior Disturbances.—Dr. H. Feldmann (*Médecine et Hygiène* 16:165, 1958) reported that changes in the personality and in behavior in children necessitates a search for causative factors. In all members of a series of 40 such children aged 7 to 17 years the author found significant emotional conflicts. Nine of the children showed disturbances in motor function, accompanied by oral fixation in 3, anal regression in 3, and nonresolution of the Oedipus complex in 2; 12 had significant ideomotor dyspraxia with dyskinesia; and on the affective plane he found poor identity in 4, anal regression in 3, and an abnormal Oedipus fixation in 3; 12 others had psychomotor instability, associated with reactional aggressivity in 7 and significant primary anxiety in 4; and 7 showed no motor disorders but had severe ego and affective disorders representing principally a reaction to a disturbing environment. For want of time and funds the children were not subjected to psychotherapy but merely to psychomotor reeducation, by means of rhythmic gymnastics, and to medical treatment. They made a progressive and gratifying adjustment to the external world. Their parents were advised as to the method of education to be adopted in each case. The speaker concluded that affectivity can develop normally only if the motoricity also develops in the same way.

TUNISIA

Radioactive Iodine and the Human Fetus.—Although among the contraindications to the use of radioactive iodine (I^{131}), pregnancy is one of the most absolute, it may be possible under some circumstances that the presence of pregnancy is not recognized and I^{131} is given to a pregnant woman with toxic diffuse goiter. Dr. G. Valensi (*Tunisie méd.* 36:69, 1958) reported such a case in a 30-year-old woman who denied being pregnant. The results of the treatment were excellent. All the toxic symptoms improved rapidly, and the exophthalmos receded markedly. The patient later reported a delay in menstruation. Her pregnancy took a normal course, and a premature infant was delivered alive in the eighth month of gestation. It weighed 2,850 Gm. (6.3 lb.), but it showed extensive malformations. The skin was thickly infiltrated as in patients with myxedema; the head in relation to the body was too large; and a pronounced exophthalmos was present. The child died half an hour after birth. It may be assumed that the thyroid of the fetus had taken up a large dose of I^{131}, in the fourth week of intrauterine life, which completely destroyed the thyroid. The absence of the thyroid hormone caused hypersecretion of the thyroid-stimulating hormone of the pituitary, thus producing the infiltration of the skin due to absence of thyroid and pronounced exophthalmos due to hypersecretion of thyroid-stimulating hormone.

UNITED KINGDOM

Poliomyelitis Vaccine.—Poliomyelitis vaccine has become a heated political issue. In a speech the Minister of Health before the House of Commons said that he proposed to import an adequate amount of Salk vaccine from the United States and Canada, without submitting it to any special tests in the United Kingdom, to supplement supplies from the two British companies that are producing the vaccine. There are three standards of safety so far as poliomyelitis vaccine is concerned. The safest is that produced in England; next comes the vaccine produced in the United States and Canada and submitted to additional tests in England; and finally comes the vaccine produced in the United States and Canada that satisfied the tests applied in these two countries but had not been tested in England. In view of the necessity for inoculating the priority classes enumerated by his experts—children under 15 and expectant mothers—the Minister, on the advice of his experts and as an emergency measure, was arranging for Salk vaccine produced in the United States and Canada to be used without additional testing. What worried many physicians was the vacillation the Ministry of Health has shown in this matter in the last two years and the effect this may have on mothers. In the first instance, the Minister declared that under no circumstances would he allow American-produced Salk vaccine to be used in this country. When this source proved hopelessly inadequate, he suddenly changed his policy and said that a limited amount of American vaccine would be imported on condition that it was submitted to stringent testing before use. Now he has again changed his policy and said that the vaccine, which up to a week or so ago, was not safe for British children can be used. The fact that he still contends that such vaccine is less safe than that being produced in this country has done nothing to allay public fears.

Duration of Night Feeding in Infancy.—In Middlesex, where demand feeding is encouraged by physicians and child welfare clinics, Janet Campbell (*Lancet* 1:877, 1958) attempted to determine how long an infant must be fed at night. No significant difference was observed between bottle-fed and breast-fed babies or between those born at home or in an institution. The important factor was weight at birth. Thus, of the 55 babies whose weight was less than 6.5 lb. (2.95 kg.) at birth, only 9% had never had a night feeding, compared with 52% of the 63 who weighed more than 8 lb. (3.60 kg.) at birth. By the age of 3 months these differences had disappeared, and by this age 91% of those with a birth-weight of less than 6.5 lb. (2.95 kg.) and 89% of those weighing more than 8 lb. (3.60 kg.) at birth had ceased their night feedings. In most cases night feeding stopped fairly suddenly. The usual story was that the baby slept through the night two or three times one week, and then the next week or the one after he no longer demanded a night feeding.

Declining Vaccination Rate.—Vaccination after birth ceased to be compulsory in Great Britain with the passing of the National Health Act in 1948. As a result only slightly more than 33% of infants are now vaccinated within the first year of life. Parents are anxious to immunize their children against diphtheria and poliomyelitis, which catch the public eye, but the threat of smallpox is not regarded seriously by parents. In Scotland the smallpox vaccination rate in the cites and towns varies from 82% to as low as 14%, in spite of propaganda drives. An inquiry showed that the most effective means of getting parents to have their children vaccinated was persuasion by the family physician and health visitor. The public are immune to overt propaganda in the form of official announcements, posters, leaflets, and the like.

Iodized Salt.—Selwyn Taylor (*Lancet* 1:751, 1958) made a plea for the use of iodized salt. The cost to the country annually of not iodizing salt as measured in terms of demands made on the medical services and loss of working time are enormous. The Medical Research Council in 1944 and again in 1948 recommended iodizing salt, as practiced in many other countries, but as yet no official action has been taken.

Sulfonamide Hematuria in Children.—In the 10 years since 1948, 29 children were treated in the medical wards of the Royal Hospital for Sick Children, Glasgow, for hematuria associated with taking sulfonamides, according to G. C. Arneil (*Lancet* 1:826, 1958). Although all subsequently recovered, anuria, hypertension, encephalopathy, and uremia were encountered in some of the patients. All but two had been given a preparation containing sulfamerazine, and in 13 of these the dosage used approximated that recommended by the manufacturer. There was no evidence that the fluid intake of these children was restricted. Despite the fact that, under ideal conditions, with a dose every 12 hours and copious fluid and alkali administration, the drug seldom produces hematuria, the overriding consideration here is that in practice this drug may cause hematuria, azotemia, and hypertension in children when given at a dosage level in frequent use. To justify giving a drug potentially toxic in therapeutic doses one must show that it has significant advantages over other preparations. Sulfamerazine appears to have no such advantages.

Hypnotism in General Practice.—According to A. A. Mason in a symposium on hypnotism reported in *The Practitioner* (180:597, 1958) hypnosis can be practiced by all, as it is easy to learn and requires no special ability or power. About 85% of the population can be hypnotized and hypnosis is an ideal anesthetic, but the deep trance necessary for this can only be produced in about 20% of all patients. On the other hand, 50% of patients may thus obtain sufficient analgesia for such minor operations as dental fillings, reduction of fractures and dislocations, and painful dressings. Hypnotism is especially valuable as an analgesic in obstetrics, giving pain relief in a high proportion of patients without interfering with labor or depressing the fetal respiratory center. Direct hypnotic suggestion aimed at symptom removal is often useful in such psychosomatic disorders as chronic skin diseases, and Mason reported a 50% recovery rate in 200 patients with previously chronic cases. Habits and such mild compulsions as nail-biting, cigarette smoking, overeating, and hiccups responded favorably. Hypnosis can be of more use to the general practitioner than to anyone except the anesthetist.

C. A. H. Watts was not so certain about this and had given up using hypnosis in his practice. He first asked why, if hypnosis is so safe and effective, it had not been widely used by the profession as a whole. After all, many conditions said to respond to hypnotism, such as asthma, enuresis, and smoking are troublesome to both the consultant and the general practitioner. He had found that the patient who will agree to this type of treatment is the exception and not the rule. Even more important than the right type of patient, in his opinion, is the right type of physician. Few doctors can stare confidently into their patients' eyes using the formula of the hypnotist. The family doctor who practices hypnotism is apt to become labelled, and this is undesirable as many people are fearful of the procedure and the physician who uses it. Frank hysteria is the ideal indication for hypnosis, but it is rarely seen in general practice, and there are usually easier alternative methods of treatment.

Alopecia due to Dextran.—The occurrence of alopecia in 8 of 15 patients treated with dextran sulfate, when the total dose was 90,000 units or more, was reported by G. R. Tudhope and co-workers (*Brit. M. J.* 1:1034, 1958). In six of these patients there was almost complete loss of scalp hair. Loss of pubic, axillary, and facial hair also occurred in three. Three of those who suffered severe loss of scalp hair were women, one of whom had complete loss of axillary and pubic hair and partial loss of her eyebrows. In all patients the hair ultimately returned to normal. The mechanism by which dextran produces its effect on hair growth is unknown, but it is suggested that it may interfere with the metabolism of the naturally occurring sulfated polysaccharides or the sulfur-containing amino acids. Diarrhea and depression of the platelet count were also encountered. This combination of toxic effects (alopecia, diarrhea, thrombocytopenia, and anorexia) is similar to the effects of whole-body irradiation and of exposure to nitrogen mustards, colchicine, and other antimitotic substances. The production of alopecia by dextran may be only one aspect of a more general and fundamental action of the drug. In spite of the advantage of good control of clotting time with infrequent injections, it is clear that, when dextran is given in a total dose of more than 90,000 units, toxicity occurs too often. No toxic effects were observed when the total dose was less than 40,000 units. Thus, 5,000 units of dextran given intravenously every 8 hours for 24 to 48 hours appears suitable as an alternative to heparin to cover the period until an orally given anticoagulant becomes effective.

MISCELLANY

CLINICAL APPLICATION OF RADIOACTIVE ISOTOPES

Radium and x-rays have been used for 60 years as a routine part of radiologic practice. The newer radioisotopes differ in no essential way except that they are artificially produced in a nuclear reactor. With proper precautions their use should be as safe, or safer.

As an indication of the popularity of isotopes, the Oak Ridge National Laboratory has dispensed over 100,000 curies of isotopes—equivalent to 200 pounds of radium (less than 3 pounds of actual radium is available in the world today).

Physical Aspects

Radioactivity implies atomic nuclear change that results in the emission of rays from the atom. A sample of a given element placed for a suitably short time in a nuclear reactor becomes transformed usually to a radioactive form of the same element. This is usually brought about by a shift in the number and relationship of the neutrons and protons in the orbit of the atom.

For example, a piece of gold foil the size of a postage stamp left for one week in a nuclear reactor becomes the equivalent, in radioactivity, of one gram of radium. In other instances one element is transformed into another. In practice, radioactive phosphorus (P^{32}) actually is made from elemental sulfur. In others the needed isotope, like radioiodine (I^{131}), is formed as an essential part of the manufacture of the atomic bomb and only requires isolation and processing.

It is essential to bear in mind that a constant fraction of the atoms of any radioisotope disintegrate or explode at a constant rate in a given period of time. If, for instance, we have one hundred atoms present at the start and find that one day later there are only fifty, we can say that its "half-life" is one day and can predict with almost absolute accuracy that at the end of two days there will be only twenty-five.

Let us then examine the different types of radiation. For purposes of general classification there are two main types: corpuscular and electromagnetic. The corpuscular types are actual particles of matter having measurable mass and moving at moderate rates of speed. They have the capacity of poor tissue penetration. Electrons (protons and neutrons), alpha particles (radium), and beta particles (radium, P^{32}, and I^{131}) are examples of the corpuscular types of radiation. Electromagnetic types differ in that they have no mass, no weight, and no charge. They move at the speed of light and have wave length and frequency. Examples of electromagnetic types of radiation would include light and have wave length and frequency. Examples of electromagnetic types of radiation would include light, radio and television, x-rays and gamma rays (I^{131}, radium, x-rays).

Clinical Applications—Diagnosis

Radioactive isotopes have made available an indispensable tool in basic scientific research as well as in the field of clinical medicine. Radioactive gold (Au^{198}) and yttrium (Y^{90}) have been used with some success in decreasing pleural effusions due to carcinoma. Radioactive phosphorus (P^{32}) is being used to treat polycythemia vera, certain leukemias and to locate intraorbital tumors. Radioactive cobalt (Co^{60}) is used to label viatmin B_{12} for a test to detect the presence or absence of the intrinsic factor in cases suspected of having pernicious anemia. Radioactive iodine (I^{131}) has found application in the diagnosis and treatment of certain thyroid disorders and in the treatment of certain types of euthyroid heart disease.

In the field of thyroid disease I^{131} is a very versatile and useful isotope. While most diseases of the thyroid can be diagnosed by history and physical examination, together with a minimal amount of laboratory work including a basal metabolic rate and serum cholesterol, there is a significant group that still offers diagnostic difficulty. The thyroid gland may be considered as a continuously running production line. Iodine is trapped, taken into the thyroid cells, utilized to form hormonal compounds (diiodotyrosine, triiodothyronine, tetraiodotyrosine), released and transported to the tissue cells. The basal metabolic rate measures the degree of cellular stimulation by measuring the metabolic rate of the cell. The radioiodine uptake measures the rate of endocrine activity of the thyroid by measuring either the degree of iodine uptake into the gland or the rate of iodine turnover, clearance, and utilization by the gland. The protein-bound iodine measures the amount of iodine that is bound to thyroglobulin as it is being transported from the gland to the tissue cells.

The technic of a radioactive iodine uptake study is quite simple. A tracer dose of radioiodine containing from 10 to 50 microcurie is given orally, and monitoring of the thyroid area at the end of twenty-four hours is accomplished by the use of a scintillation counter. Standards are likewise counted and calculations are made, based on the amount of radioactivity given. The percent uptake of the radioactive material by the thyroid is determined

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Condensation of an article by Ben D. Hall, M.D., presented before the Tennessee Regional Meeting, American College of Physicians, Paris Landing, Tenn., Oct. 19, 1957, and published in the *Journal of the Tennessee State Medical Association*, April, 1958.

with a standard formula. In general, uptakes from 0 to 15% are indicative of hypothyroidism. Uptakes from 15 to 45% indicated euthyroidism. Uptake values between 45 and 50% are considered borderline, and uptakes above 50% indicate hyperthyroidism. . . .

Previous treatment with inorganic iodides such as Lugol's solution or potassium iodides will result in a falsely low value. This is likewise true for the organically bound iodine utilized in intravenous pyelograms, myelograms, cholecytograms, etc. The prior use of goitrogenic drugs, such as propylthiouracil, will likewise invalidate the accuracy of the test unless the drug has been discontinued for a period of time prior to the test.

In cases where the iodine uptake is borderline normal, other tests may be desirable. In certain cases a thyroid clearance test may be helpful. This measures the rate of clearance of the iodine from the blood by the thyroid. The radioiodine is given intravenously and periodic measurements of the thyroid gland and the plasma are made at specific intervals. Results are expressed as milliliters of plasma per hour cleared of radioiodine by the thyroid gland.

The chemical measurement of the protein-bound iodine is highly technical and not widely available. However, after a suitably high tracer dose of I^{131} is given, that portion of iodine bound to protein can be detected in a well counter and the percentage of organically bound iodine can be determined. This is done either by precipitating the protein fraction or by removing the inorganic portion by absorption onto a resin column. This gives the protein-bound iodine conversion ratio which is of diagnostic value in some cases where the iodine uptake is in the borderline range.

Another test of value is the thyroid suppression test. In certain instances where the original uptake value is of borderline elevation, the patient is given large doses of desiccated thyroid or triiodothyronine for 10 to 14 days to suppress thyroid function. The 24 hour uptake is then repeated. If the gland is truly overactive no significant reduction in uptake is observed. If the gland is basically euthyroid the second uptake will be significantly lower than the first.

In addition to uptake studies the gland may be scanned for the study of thyroid nodules. This may be done by the use of a handheld probe or by the use of a mechanical device which may actually record a scintogram of the gland. In 1940, Hamilton, Soley, and Eichorn, using radioautographic studies of thyroid tissue slices, found that cancerous tissues retain practically no radioiodine whereas normal thyroid tissue concentrated large amounts of the isotope. Cope, Rawson, and McArthur, and several others working independently reported that benign hyperplastic nodules concentrated more radioactive iodine than normal tissue. . . . In general it may be stated that malignant nodules do not pick up radioiodine and will be "cold" as far as selective counting is concerned. Metabolically inactive thyroid tissue, due to any cause, likewise will be "cold" (hemorrhagic cyst, areas of thyroiditis, calcification, fibrosis, etc.). Hyperplastic nodules will concentrate more radioiodine than will contiguous tissue and can be identified accurately. This technic has limited application in the therapy of nontoxic nodular goiter by the use of thyroid feeding with large doses of desiccated thyroid in an attempt to suppress pituitary thyroid-stimulating hormone. . . .

Treatment

Radioiodine treatment is indicated in the following circumstances: (1) uncomplicated hyperthyroidism over age 40; (2) recurrent or persistent postoperative toxicity; (3) toxicity in poor surgical risk patients; (4) idiosyncrasy to antithyroid drugs; (5) refusal to accept surgery; and (6) severe or progressive exophthalmos.

Treatment with radioactive iodine may be considered contraindicated in the following circumstances: (1) uncomplicated hyperthyroidism under age 40; (2) toxicity in children; (3) pregnancy or lactation; and (4) large toxic nodular goiters.

The advantages of oral treatment with radioactive iodine are obvious. No hospitalization is necessary. There is no operative mortality, discomfort or scar, and there is no danger to the recurrent laryngeal nerve or parathyroid glands. Inasmuch as treatment may be given on an outpatient basis, there is minimal loss of time from work and minimal expense.

Treatment is given orally on a fasting stomach. The dosage is designed to deliver to the gland between 100 and 140 microcurie per gram of gland, or to deliver between 5,000 and 10,000 roentgen equivalent physical (rep). There are as many methods of estimating dosage as there are groups giving therapy. In general the results reported are similar—85% are euthyroid after one or more treatments. The incidence of post-treatment hypothyroidism varies between 4 and 18 percent. As a general rule those who tend to give low initial doses will have a higher incidence of retreatments but will have a lower incidence of post-treatment hypothyroidism. The most important factor in determining the dose is clinical judgment. This includes factors such as the size of the gland, the presence or absence of nodules, the clinical degree of toxicity, the percent uptake at the end of twenty-four hours, the age of the patient, and the presence of associated but related disease.

We have utilized the following modified Quimby formula for calculation of the dosage designed to deliver from 5,000 to 10,000 rep:

I^{131} to deliver 1,000 rep = weight of gland × 0.0555 ÷ the percentage uptake times the biologic half-life.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Problem of Chronic Pneumonia. K. G. Nikulin. Klin. med. 35:46-50 (Dec.) 1957 (In Russian) [Moscow].

Chronic pneumonia is a poorly defined but a rather frequent entity. It is commonly regarded as a manifestation of pneumosclerosis. The author insists that chronic pneumonia must be regarded as the primary and pathogenetic basis of pneumosclerosis, bronchiectasis, and pulmonary suppuration. Chronic pneumonia can be primary or secondary—the result of an acute pneumonia. It runs a protracted, undulant course with subfebrile temperature and sometimes without physical manifestations. The clinical picture becomes manifest with the development of bronchiectasis or of suppuration. Chronic pneumonia is resistant to antibiotics and to sulfanilamides. Its treatment, therefore, must be directed to the improvement of the general health, repeated blood transfusions, and vitamin administration. Chronic pneumonia complicated by bronchiectasis or suppuration must be treated surgically.

Comparative Study of Treatment with Hormones, Salicylates, and Phenylbutazone on the Basis of 631 Cases of Acute Rheumatic Fever Observed in Four Years (497 in Children). J. Chevallier. Rev. rhumat. 25:1-17 (Jan.) 1958 (In French) [Paris].

The records of 631 patients with acute rheumatic fever treated during the period from 1953 to 1956 in 13 hospital services were reviewed and compared in relation to the 3 forms of treatment received. Sodium salicylate and aspirin were identical in their effect, lowering the erythrocyte sedimentation rate to a normal level within 5 or 6 weeks. Similarly, equivalent doses of the various hormones (corticotropin, cortisone, hydrocortisone, and deltacortisone) produced identical effects. The lowering of the erythrocyte sedimentation rate took place more rapidly in patients receiving the hormones than in those receiving salicylates (2 to 3 weeks instead of 5 or 6), but it was often accompanied by a transient hypofibrinemia. Phenylbutazone, the third form of treatment, had only a slow and incomplete effect on the erythrocyte sedimentation rate. The rebound of the rate, which is habitual after hormone treatment and which occurs fairly often after the administration of salicylates, seems to be rare in patients who have been treated with phenylbutazone. Leukocytosis returns to normal in 3 weeks under treatment with salicylates or phenylbutazone, but in patients receiving hormones this effect is produced more slowly. The course of the heart murmurs in the various therapeutic groups suggests that hormone treatment is superior to treatment with salicylates, but the number of patients is too small and the follow-up is too short for any definite statement to this effect. The effect of phenylbutazone on rheumatic carditis is an important finding, because it is in contrast to its mediocre effect on the erythrocyte sedimentation rate. Each of the 3 forms of treatment gives rise to certain complications, the most severe of which are occasional psychic disturbances in patients receiving cortisone or cortisone derivatives and hemorrhages of various kinds in patients receiving phenylbutazone.

Hormone administration, on the basis of this study, is regarded as the best treatment now available and the one that is the easiest to manage, especially when deltacortisone is used: it has the widest margin of safety between a useful and a toxic dose. Phenylbutazone seems to produce equally brilliant results, but complications are frequent and sometimes serious. Aspirin is apparently less effective so far as carditis is concerned; in addition, the fact that it has to be given in large doses, to the limit of tolerance, makes its use inconvenient.

Sarcoidosis and Tuberculosis. I. Ståhle. Nord. med. 59:302-303 (Feb. 20) 1958 (In Swedish) [Stockholm].

Sarcoidosis and tuberculosis can occur in different combinations: 1. Tuberculosis, usually grave, develops slowly after primary sarcoidosis. 2. After a symptom-free period that follows an apparently healed tuberculous lymph-node or parenchyma process, a typical sarcoidosis develops without signs of activity of the tuberculous changes. 3. An active pulmonary tuberculosis passes directly into sarcoidosis with disappearance of the positive tuberculin reaction. Two cases of type 3, which is rare, are presented. In both cases the disease began

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The place of publication of the periodicals appears in brackets preceding each abstract.

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as pulmonary tuberculosis, with positive tuberculin reaction and tubercle bacilli demonstrated in the sputum. In the first case unilateral pulmonary sarcoidosis gradually developed, with negative Mantoux reaction, after an interval with weakened positive tuberculin reaction and, simultaneously, bacteriologically established tubercle bacilli and histologically certain diagnosis of sarcoidosis. Microscopic examination of resected, formerly tuberculous segments showed only typical sarcoid structures. In the second case cutaneous sarcoidosis developed together with bilateral pulmonary sarcoidosis. The changes showed good regression on treatment with vitamin D (Fortedol). This treatment should be given in hospital with close control of the renal function. It is considered likely that long-term antituberculosis treatment, especially with isoniazid, may induce a change in the tubercle bacilli with subsequent development of sarcoidosis. Bronchoscopy with biopsy seems to be indicated in sarcoidosis.

Environmental Penicillin and Penicillin-Resistant Staphylococcus Aureus. J. C. Gould. Lancet 1:489-493 (March 8) 1958 [London].

The proportion of penicillin-resistant strains of Staphylococcus aureus is increasing in hospitals among carriers who are not receiving penicillin. This is usually explained by postulating a free interchange of organisms between the treated patients and these carriers, but this presupposes that the penicillin-resistant organisms have the power to replace the naturally occurring penicillin-sensitive carrier strains. So far there is no satisfactory evidence that this happens. Further, if mutation takes place in each patient under treatment, a much greater variety of phage types of penicillin-resistant staphylococci would be expected to occur in hospitals, whereas it is usual for only a few strains to be present in each hospital. Also, patients infected with penicillin-sensitive strains before treatment would be expected to yield penicillin-resistant strains of the same type after treatment. In fact, most patients who are investigated show the penicillin-resistant strains to be of different type from the sensitive strains originally present. Another possible explanation of the rapid colonization among carriers in hospital is that these persons receive in their noses enough penicillin, inhaled with air and dust and transferred from their hands and fingers, to maintain a nasal concentration of penicillin inhibitory to sensitive staphylococci. Evidence for this hypothesis was sought by testing the environment in a hospital for free penicillin and comparing the results with those found in a factory handling penicillin.

The hospital examined was a large general hospital with about 900 physicians and nurses. Permanent nasal carriers comprised 53% of the staff, and the proportion of these carriers harboring penicillin-resistant strains exceeded 90%. The factory examined handled penicillin from bulk and dispensed it in various forms. The amount of penicillin recovered in different parts of the hospital varied considerably but was greatest nearest those rooms where penicillin was being handled or therapeutically administered. Leakage from the phial during puncturing, clearing of air bubbles and froth from syringe and needles, and spraying when washing out the syringe commonly takes place during the process of injecting a patient. Air may be contaminated in 2 ways: directly, by droplets atomized from syringes and the like, and indirectly, by the raising of dried spilt penicillin as dust. The hospital environment can, therefore, readily acquire penicillin, and the amount may be cumulative, because destruction of the dried penicillin in dust may be relatively slow, and the penicillin would continually be redistributed through disturbances of dust and air and the handling of articles.

Appreciable amounts of penicillin were shown to gain access to the nares of persons working in the hospital environment, and without doubt this will inhibit the growth of penicillin-sensitive strains of Staphylococcus aureus. Such persons will be continually exposed to recontamination with staphylococci from the environment, the great majority of which in hospital will be penicillinase-producing strains. Penicillin-resistant strains will, therefore, find it easy to establish themselves and to colonize the nares of a larger number of persons in hospital than in environments which do not contain penicillin. The environment of the factory handling penicillin was similar to that of the hospital in that it contained penicillin and all the carrier strains of Staph. aureus were penicillin-resistant. Environmental penicillin is an important factor in the colonization of hospital nasal carriers with penicillin-resistant Staph. aureus and in the cross-infection of persons receiving or not receiving penicillin therapeutically.

Changes in the Level of Serum Glutamic Oxaloacetic Transaminase in Myocardial Infarction. P. Fortin, R. Bourdon, J. van Vonterghem and Y. Bouvrain. Bull. soc. méd. hôp. Paris 74:9-20 (No. 1 and 2) 1958 (In French) [Paris].

Measurements of serum transaminase activity were made by the authors in 9 patients hospitalized for a painful thoracic syndrome that had led to a diagnosis of myocardial infarction. Their findings were in harmony with those previously reported by others. The level of transaminase was almost always increased, and the results differed little from patient to patient. The rise in the serum glutamic oxaloacetic transaminase took place early, within the first 24 hours and usually about the 6th hour. The level reached a maximum of 2 to 10 times the normal 24 to 48 hours after onset, returning to normal rapidly and constantly on the 5th or 6th day. Myocardial infarction is not the only condition in which there is an increase in the serum glutamic oxaloacetic transaminase level; in particular, care must be taken to ascertain that the patient is not in a state of hepatic insufficiency. The diagnostic significance of increased serum transaminase in myocardial infarction, however, is indisputable, especially in difficult cases, such as those involving extension of a recent infarct or those in which the presence of earlier lesions makes it hard to interpret the electrocardiographic tracings. The measurements should be made as soon as the condition is observed, and they should be repeated daily, if possible, up to the 8th day. A rise in the serum transaminase is less valuable from the prognostic point of view, because, although the amount of the increase is apparently proportional to the extent of the necrosis, the size of the infarcted area is not the only element affecting the prognosis in patients with myocardial infarction.

Action of a Preparation of Gastric Mucin in Lowering Serum Concentrations of Lipids. L. Cucurachi and A. G. Dettori. Minerva med. 48:4503-4512 (Dec. 26) 1957 (In Italian) [Turin, Italy].

Variations in serum concentration of lipids and cholesterol produced by a preparation of gastric mucin were studied in 3 groups of a total of 40 hospitalized patients of both sexes, between the ages of 36 and 72 years. The first group consisted of 12 patients with diabetes associated with atherosclerosis, the second group consisted of 18 patients who had general atherosclerosis with prevalent myocardial localization, and the third group consisted of 10 patients with various disorders, such as obesity, glomerulonephrosis, and essential hypertension. The preparation was given orally, in 3 divided doses of 100 mg. each, after meals for a period between 20 and 40 days. Determinations of total serum cholesterol, cholesterol esters, fatty acid, and, in some instances, phospholipids were made in patients in fasting state 10, 20, 30, and 40 days after beginning of the treatment. The preparation brought about gradual decrease of total serum cholesterol, cholesterol esters, and fatty acid values during the treatment, which was already noted at the first test taken 10 days after beginning of the treatment. These values tended to increase after discontinuance of the therapy. Since the preparation of gastric mucin was well tolerated by the patients, the authors suggest its use for prolonged periods of time.

The best results were noted among the patients with diabetes; all responded to the treatment in varying degrees. Patients with general atherosclerosis showed less or no response. Patients of the third group showed the least satisfactory results. Mean decrease of fatty acid values was larger than mean decrease of total serum cholesterol values in the first 2 groups. The preparation of gastric mucin has thus proved to have the effect of normalizing the serum concentrations of lipids and cholesterol.

Variants of Kartagener's Syndrome in the Same Family. E. L. Overholt and D. F. Bauman. Ann. Int. Med. 48:574-579 (March) 1958 [Lancaster, Pa.].

The authors report on a family consisting of 6 members, the 40-year-old father, the 39-year-old mother, 2 sons aged 13 and 8 years, and 2 daughters aged 14 and 5 years, 5 of whom had incomplete forms of the syndrome described by Kartagener as the triad of situs inversus, bronchiectasis, and chronic sinusitis. The father had only chronic sinusitis, and the mother had always been in good health. The 14-year-old daughter had agenesis of the frontal sinuses, underdeveloped paranasal sinuses, sinusitis, nasal polyposis, and bronchiectasis without dextrocardia; she did not have bronchiectasis when a bronchogram was made at the age of 6. The 5-year-old daughter had complete situs inversus, sinusitis, underdeveloped paranasal sinuses, chronic bronchitis, and fibrosis of the lower lobe of the left lung; she did not yet have bronchiectasis. The 2 boys had sinusitis only. It appears that bronchiectasis and sinusitis are acquired, although the familial tendency indicates a definite antenatal influence. The exact nature of the respiratory defect or the manner of inheritance is not clear on reviewing the literature. In the families described by other workers and by the authors, it is apparent that Kartagener's syndrome can occur in various combinations within the same family. The importance of early recognition and prompt therapy is reemphasized.

Serologic Diagnosis of Brucellosis: Certain Effects of Epinephrine. G. Frada, Minerva med. 48:4493-4499 (Dec. 26) 1957 (In Italian) [Turin, Italy].

Experiments have shown that epinephrine often produces an increase in value of the Wright agglutination test or elicits a positive from a previously negative agglutination test. This phenomenon has induced the author to use epinephrine during the past few years. The case of a woman, 45 years old, who had a chronic form of brucellosis is presented. The first clinical signs of the disease appeared 2 years before admission to the clinic. The disease had never been completely cured, and intermittent febrile periods occurred. This was probably due to incongruous antibiotic medication. On admission, treatment with epinephrine in daily dosage of 1/50 mg. administered intravenously for several weeks was instituted. Before the injection the agglutinin titer was 1:320; it rose to 1:1280 5 minutes after the injection during the first few days of treatment. The increase in agglutinin titer was accompanied by the paradoxical phenomenon with the prozone ranging from 1:10 to 1:320. These readings were unaltered after heating the serum at 56 C for 30 minutes. After several days of treatment, the agglutinin titer decreased to 1:320 both before and after the injection of epinephrine, and the paradoxical phenomenon disappeared. The spleen was enlarged on admission, but its size was reduced to physiological limits at the end of the epinephrine therapy. The patient was free from all symptoms of brucellosis after termination of the therapy.

Familial Ulcerative Colitis and Ileitis. E. A. W. Houghton and J. M. Naish. *Gastroenterologia* 89:65-74 (No. 2) 1958 (In English) [Basel, Switzerland].

The authors report on 7 families from the Bristol area in England, in which there were 14 proved cases of ulcerative colitis and 4 cases of regional ileitis. Two members of 3 families and 3 members of 1 family had ulcerative colitis. Of 2 brothers in 1 family, 1 had ulcerative colitis and 1 regional ileitis. In 1 family of 3 generations, 4 members had ulcerative colitis and 1 had regional ileitis. In the 7th family, 2 members had regional ileitis for which an ileotransversostomy was performed, after which there was a recurrence with involvement of the colon. From an analysis of hospital admissions in the Bristol area, an estimate was made of the incidence of the 2 diseases in the general population; it showed a rate of 0.85 per 1,000 for ulcerative colitis and a rate of 0.14 per 1,000 for regional ileitis. These data strongly suggest that the reported familial incidence is not coincidental. It seems safe to assume that a hereditary predisposition exists for both diseases and that it is not possible to draw a sharp dividing line between ulcerative colitis and regional ileitis. The hereditary factor, together with the variability of the clinical picture, the occurrence of mild cases, the frequently relapsing course, the wide range of histological findings, and the suppressive effect exerted by corticoid preparations, makes an allergic basis likely in both diseases.

Jaundice, Hyperlipemia and Hemolytic Anemia: A Heretofore Unrecognized Syndrome Associated with Alcoholic Fatty Liver and Cirrhosis. L. Zieve. Ann. Int. Med. 48:471-496 (March) 1958 [Lancaster, Pa.].

Twenty men, between the ages of 26 and 65 years, with alcoholism, who were observed at the Minneapolis Veterans Administration Hospital in the course of the last 8 years, showed an interesting group of manifestations heretofore not recognized as a distinct syndrome with a predictable course. Anorexia, nausea or vomiting, diarrhea, and weight loss were common. Malaise, weakness, cough, and chilliness were also frequent. Upper abdominal pain was almost always present but varied in severity. Low-grade fever lasting several weeks after admission was the rule. Tremulousness was common, and frank delirium tremens occurred occasionally. The essential clinical features were jaundice, hyperlipemia or hypercholesterolemia, and hemolytic anemia. The illness followed excessive drinking, and improved rapidly once the drinking stopped. The hyperbilirubinemia and hypercholesterolemia receded over a few weeks. Hemolysis was generally slight and of short duration. The anemia was mild and did not persist. Hepatic function was usually mildly disturbed and improved rapidly. Liver biopsy specimens were obtained from 16 patients; fatty infiltration was evident in the livers of 14 patients, and minimal to moderate portal cirrhosis in those of 15 patients.

The patients generally presented diagnostic problems until the syndrome was defined. Obstructive jaundice was often suspected initially, and exploratory laparotomy was performed on 1 patient. The anemia was always recognized; however, hemolysis was usually not suspected. Repeated examinations of stools for occult blood were made, with negative findings. In 1 patient the hemolytic anemia was extensively studied without recognition of the related alterations in blood lipids or in hepatic function. The mechanism of the hemolytic anemia is unknown. The hemolysis seems to be related to the hyperlipemia, and an abnormal lipid may be present.

Tetanus of the Adult in the Hospital Civil of Guadalajara: Clinical Picture and Treatment. A. Ruiz Sánchez and F. Ruiz Sánchez. Arizona Med. 15:103-104 (Feb.) 1958 [Phoenix].

The authors report on 42 men and 23 women with tetanus, who were treated at the Hospital Civil of Guadalajara, Mexico, between 1952 and 1957. Most of the patients were between the ages of 10 and 50 years. Seventeen of the 65 patients died within the first 36 hours of treatment. The period of incubation varied from 1 to 4 days up to 2 or 3 months. In general, the shorter the period of incubation, the more severe the clinical picture. The clinical picture was characterized by tonic tetanic spasms of the muscles of mastication and the spinal muscles. Trismus was present in 45 (93%) of the 48 patients who survived the first 36 hours of treatment. Subintrant paroxysms were observed in 44 (92%), opisthotonos in 39 (81%), rigidity of the nape of the neck in 36 (75%), and fever in 42 (87%). Patients with a consistently high fever died.

Treatment was practiced as follows. For the first 3 to 6 days 60,000 to 100,000 units of tetanus antitoxin was given, but evaluation of its effect was not possible, since the course of the disease in the patients who did not receive tetanus antitoxin did not differ from that in the patients who were treated with tetanus antitoxin. Chemotherapy consisted of administration of penicillin and streptomycin and was combined with supportive treatment, including relaxing agents, sedatives, cardiovascular stimulants, administration of fluids, and administration of oxygen when needed. Attention was paid to the air passages, and tracheotomy was performed when necessary. For cortical sedation, chlorpromazine hydrochloride was given in doses of 25 mg. once or twice a day by the intramuscular route. It apparently produced a better sedation than the barbiturates, which were used in 29 patients and were given in doses of 0.15 to 0.30 Gm. intramuscularly every 6 hours in the early stage of the disease and once or twice a day thereafter. The use of diphenhydramine (Benadryl) hydrochloride by either the oral or the intramuscular route in doses from 50 to 200 mg. has been considered advisable.

In the group of patients treated for more than 48 hours, the mortality was reduced to 33%. If the patients who died within the first 36 hours were included, the mortality rate was 50%. In general, mortality was higher in women patients between the ages of 20 and 30 years, in those in whom the portal of entry was through a wound produced by a sharp instrument or hypodermic needle, in those with a short incubation period, and in those with a severe clinical aspect. The predominant complications were of two types, those related to the illness itself, such as respiratory paralysis, laryngeal spasm, asphyxia, heart failure, etc., and those which occurred as a result of treatment, the anaphylactic reactions and oversedation in those patients with respiratory complications.

Vitamin B_1 Treatment of Gastric and Duodenal Ulcer. V. I. Ivanov-Neznamov. Klin. med. 36:133-139 (Jan.) 1958 (In Russian) [Moscow].

The author treated 158 patients with gastric ulcer and 184 patients with duodenal ulcer with vitamin B_1. A control group, treated dietetically only, consisted of 30 patients with gastric ulcer and of 77 patients with duodenal ulcer. Investigation of the presence of vitamin B_1 in 150 patients with gastric ulcer showed its deficiency in 73.3%. One hundred fifty patients with duodenal ulcer showed deficient vitamin B_1 in 69.3%. Forty-two patients with either gastric or duodenal ulcer showed, together with deficient vitamin B_1 in the 24-hour specimen of urine, an increase in pyruvic acid. Clinical, roentgenologic, and gastroscopic studies of the material established the healing of the gastric ulcer in 92% and of the duodenal ulcer in 86%. Clinical and anatomic healing of the gastric and the duodenal ulcer in the control group was observed in only 40.4% of the patients.

Vitamin B_1 therapy shortened the hospital stay of the patients from the usual 45-50 days to 32-35 days. Vitamin B_1 is more effective in the treatment of ulcerative disease in doses of 25 mg. given subcutaneously 2 to 3 times daily in the course of 30 to 35 days. The diet is of the mechanical and chemical sparing type. Animal albumin in the amount of 2 Gm. per kilogram of weight helps correct vitamin B_1 hypovitaminosis. Clinical, roentgenologic, and gastroscopic observations showed that the duration of cure of ulcer disease under the influence of vitamin B_1 does not exceed the average of 32 days for ulcer of the stomach and 35 days for ulcer of the duodenum. Painful ulcer syndrome disappears, as a rule, during the first 3 to 5 days of the treatment; dyspeptic and gastric manifestations disappear during the first 6 to 8 days. Gastric acidity increases in antacid and subacid gastritis and diminishes down to normal figures in hyperacid gastritis. The gastroscopic appearance of gastritis becomes normal more often in gastric ulcer, even though the gastritis persists longer than the ulcer. Recurrences have been noted in not more than 15% of the patients. They were somewhat more frequent in those with duodenal ulcer.

SURGERY

Lingular Disease Simulating the Right Middle Lobe Syndrome: Report of a Case. D. E. Storey. J. Indiana M. A. 51:303-309 (March) 1958 [Indianapolis].

The author reports on a 40-year-old woman with 2 attacks of pneumonitis at an interval of 6 weeks, for which she was given antibiotic therapy; this resulted in the disappearance of symptoms but not in the clearing of a lesion in the lingular segment of the upper lobe of the left lung, shown by the chest roentgenogram. Two months later the patient again had pain in the left side of the chest, a cough productive of yellow purulent material, rise in temperature to 99.4 F (37.5 C), and considerable clouding of the lingular segment on roentgenologic examination. Bronchoscopy did not show significant abnormal findings in the right and left main bronchi, but there was a moderate amount of mucopurulent exudate aspirated from the region of the lower lobe orifice. Thoracotomy was performed, and on opening the pleural cavity on the left the lingular portion of the left upper lobe was found to be atelectatic and involved in a chronic suppurative process. During dissection of this, an obstructive broncholith, measuring about 1.5 cm. in diameter, was found in the superior branch of the lingular bronchus. The lingular portion of the left upper lobe was removed. There were no other significant gross abnormal findings in the left lung. The clinical picture and roentgenologic findings were considered to be the result of chronic obstruction due to the presence of the concretion. Pathological examination of the surgical specimen revealed pneumonitis and bronchiectasis. The postoperative course of the patient was uneventful, and for about 2 years after the operation she had no recurrences of her respiratory symptoms and no further attacks of pneumonitis.

A review of the Anglo-American literature for the past 10 years and pertinent papers before that time failed to reveal any cases of isolated lingular disease due to an obstructive broncholith. The middle-lobe syndrome and its symptom complex are well recognized, and the possibility of the diagnosis is always considered whenever disease occurs in the lower chest on the right. Isolated lingular disease with a similar symptom complex is definitely less well known and apparently seldom recognized. The causation of isolated lingular disease is probably not as variable as that of the middle-lobe syndrome, but still the condition is presumably due to either intraluminal or extraluminal causes, such as are seen in the middle-lobe syndrome. The anatomy of the middle-lobe bronchus and the anatomy of the bronchus to the lingular segment of the left lung are definitely different, and this fact explains the definitely smaller number of isolated cases of lingular disease. As in the case of the middle-lobe syndrome, the definitive diagnosis of isolated lingular disease can be made only by surgery and after examination of the resected specimen. Clinical bronchoscopy and roentgenologic findings are important in the preoperative preparation of the patient, but a definitive diagnosis cannot be made on these findings alone.

Results of Surgical Treatment for Carcinoma of the Stomach at Denk's Clinic in Vienna. H. Denk and F. Helmer. Gastroenterologia 89:19-37 (No. 1) 1958 (In German) [Basel, Switzerland].

Of 863 men and 566 women, between the ages of 21 and over 80 years, with carcinoma of the stomach, 1,246 (87.2%) were operated on at the second surgical clinic of the University of Vienna, and 97% of them were followed up between 1933 and 1955. The results of surgical treatment obtained in these patients were critically examined. In 63.1% of the patients complaints had existed for a longer period than 3 months before admission to the clinic. Forty-six per cent of the patients disregarded the early symptoms, and in 54% the physician-in-charge failed to make an early diagnosis. Of the 1,246 patients operated on, 372 underwent an exploratory laparotomy, and 256 had palliative operations (gastroenterostomy and gastrostomy). Six hundred eighteen patients (43%) had gastric resection. The primary operative mortality rate after subtotal resection, according to Billroth 1 or 2, was 16.8%, after resection of the gastric cardia 32.5%, and after total gastrectomy 33.6%. Almost 50% of the deaths were caused by insufficiency of suture and peritonitis. Of the 618 patients with total resection, the operation was not radical in 29, i. e., it did not include resection of lymph-node metastases. Of the remaining 589 patients, 126 died and 463 were discharged: 43 of these could not be traced, which left 420 patients who were followed up. Sixty-seven and five-tenths per cent died within 1 year after the operation, 46% within 2 years, and 28% within 5 years.

As to postoperative results, patients with corpus carcinoma have the most favorable life expectancy, while those with carcinoma consisting entirely of connective tissue and with carcinoma of the cardia have the least life expectancy. The tumors with localized growth (types 1 and 2), according to Borrmann's classification, have a 50% better prognosis than the infiltrating carcinomas (types 3 and 4). The incidence of recurrence of the tumor in the anastomosis and in the stump, respectively, was 16% in the patients with type 1 and type 2 carcinoma and 84% in those with type 3 and type 4 carcinoma.

Concerning postoperative functional disturbances in the absence of recurrence, the patients were divided into 4 groups: those who were completely free of complaint (83.4%); those with mild complaints which could be relieved by diet alone (13%); those with moderate complaints despite adequate diet (1.8%); and those with severe complaints (1.8%). A dumping syndrome was observed in 31%, regurgitation in 35%, and vomiting in 4%. Dysphagia was observed in 50% of the patients who had undergone total gastrectomy and esophagojejunostomy and in 20% of those with resection of the cardia. These data suggest that reflux of the chyme, particularly in the presence of disturbance of motility, rather than regurgitation of the acid gastric juice, may be responsible for the dysphagia. The authors' findings show that from the practical point of view total gastrectomy does not provide substantial improvement in prognosis. Total gastrectomy is indicated only in patients with the infiltrating forms of carcinoma of the stomach (Borrmann's types 3 and 4) without lymph-node metastasis (relative indication) or in those in whom the size of the tumor makes it imperative (absolute indication).

Emergency Gastrectomy for Acute Gastroduodenal Perforation. E. J. Cerise. J. Louisiana M. Soc. 110:67-71 (March) 1958 [New Orleans].

In January, 1953, a deliberate change in the policy of management of acute gastroduodenal perforation was made by the surgical service in Tulane University School of Medicine at Charity Hospital of Louisiana in New Orleans. This change consisted in the performance of immediate subtotal gastrectomy instead of simple closure in all suitable cases. Only the good-risk patients were submitted to gastrectomy, whereas, the more critically ill were treated by simple closure. From January, 1953, through May, 1957, there were 96 patients on the Tulane surgical service treated by surgical measures. Of these, 46 had simple closure of their perforation, with 6 deaths, a mortality rate of 13%. The remaining 50 patients had subtotal gastrectomies, with 1 death or a 2% mortality rate. This 1 death resulted from a transfusion reaction. The 50 gastrectomies were regarded as technically easy, as the associated edema often facilitated the dissection. However, in 2 instances, due to the reaction and scarring in the area, tube duodenostomy was necessary. The standard Billroth 2 technique was usually followed.

One of the 46 patients treated by simple closure began to bleed shortly after operation and required emergency gastrectomy on the 6th postoperative day for control of hemorrhage. This case deserves special mention, because it emphasized the possibility of simultaneous acute peptic ulcers on the anterior and the posterior wall of the duodenum. In the 50 gastrectomies, an additional posterior ulcer was noted in 7 cases. This incidence of at least 14% multiple ulcers is recently becoming appreciated in perforations with hemorrhage. The author lists the following as absolute indications for gastrectomy in acute perforations: (1) carcinoma of the stomach (delimited resectable lesions); (2) associated with recent or simultaneous gross hemorrhage; and (3) associated with fixed pyloric obstruction. In addition, from the knowledge gained by follow-up studies, the author regards the following as justifiable indications: (*a*) recurrent perforations and (*b*) a definite previous ulcer history (more than 6 months) and in the younger age groups (under 50 years). The author concludes that a more aggressive attitude than simple closure is necessary, but the routine use of gastric resection seems unwarranted. It is suggested that certain criteria based on the condition of the patient and his prognosis be used to determine the appropriate treatment.

Treatment of Endarteritis Obliterans by Intra-Arterial Blood Infusion. N. V. Rozovsky. Khirurgiya 33:53-59 (No. 12) 1957 (In Russian) [Moscow].

This method of treating endarteritis obliterans consisted of infusing from 200 to 250 cc. of blood into the femoral artery of the patient under a pressure of 40 to 60 mm. Hg higher than the patient's blood pressure. The infusion was performed 2 to 4 times, with an interval of 5 to 6 days. The treatment given to 101 patients gave considerable improvement in 66%, some improvement in 25%, and no improvement in 9%. Good results were obtained principally in young patients. Adults with pronounced arteriosclerosis were not benefited by this treatment. In the younger patients the extremities after intra-arterial blood infusion became warm and of normal color. There was considerable improvement in the circulation in the extremities and in the myocardium and also in the electrolyte content and the viscosity and coagulation time of the blood. A follow-up ranging from 6 months to 6 years in 71 patients revealed recovery or pronounced improvement in 25%, improvement in 12.3%, relapse in 11.6%, amputations in 4.4%, and lethal outcome in 6.5%. A number of patients will require repeated blood infusions after a lapse of time.

Acute Forms of Regional Enteritis (Diagnosis and Treatment). M. P. Détrie. J. chir. 75:156-174 (Feb.) 1958 (In French) [Paris].

Acute terminal ileitis may appear in any of the 3 well-known clinical forms and in a less common but severe form called the necrotizing form. The pseudoappendicular form is benign and corresponds to a simple edematous lesion; the symptoms suggest acute appendicitis, but the condition may be differentiated by the occurrence of diarrhea, which is rare in ordinary adult appendicitis but is characteristic of terminal ileitis. This form of the disease frequently undergoes resolution, but in patients over 30 years of age it may be the prelude to a prolonged chronic condition. The peritoneal form, producing the picture of peritonitis due to perforation, which may or may not be present at operation, is rarer and much more severe, as shown by the occurrence of 4 deaths in 1 series of 10 cases. The occlusive form with acute obstruction of the terminal small intestine is rare. Its onset is characterized by violent pains progressing to paroxysmal attacks. Diagnosis is facilitated by the inflammatory course of the occlusion, which progresses with fever and a certain amount of abdominal contraction. Other forms of acute regional enteritis are those affecting the jejunum, the cecum, the duodenum, and the colon, either separately or in various combinations. The postappendicular form is one in which a clinical pseudoappendicular syndrome was not recognized at the time of appendectomy. Surgical treatment does not always provide protection against renewed acute attacks of the disease; recurrences, in fact, are characteristic of regional enteritis.

The diagnosis of regional enteritis is not easy. Whatever the clinical aspects, 3 factors will prove helpful in making the diagnosis: the youth of the patient, diarrhea, and an earlier appendectomy. Roentgenography may result in visualization of pneumoperitoneum in cases of perforation and may reveal the presence of fluid in patients with occlusion. Conditions requiring differentiation are acute appendicitis, typhoid, intestinal infarct, simple ulceration of the small intestine, secondary ileitis, intestinal tuberculosis, and Hodgkin's disease. Medical treatment is often disappointing, but antibiotics may be useful in complications such as peritonitis, abscesses, and fistulas, although they have no effect on the disease itself. Administration of cortisone or corticotropin (ACTH) sometimes produces a transient cure, but this has little value in a disease characterized by recurrent attacks. Perforation and hemorrhage are sometimes caused by these hormones. Surgical treatment ranges from simple exploratory laparotomy to resections of various kinds according to the site of the lesion. Surgical treatment is not indicated when the diagnosis of the appendicular form is made before operation, but if the diagnosis is made during laparotomy, the operation should be limited to a simple survey of the lesions, and no resection or short-circuit procedure should be attempted. Resection in spite of a fairly high mortality is possibly the best procedure in cases of perforating or necrotizing enteritis. The occlusive forms require emergency treatment, such as resection, simple freeing of the loop, or internal or external derivation, depending on the general condition of the patient and the change in the intestinal segment. Various special operations, such as gastrojejunostomy, may also be used with good effect in certain localizations.

Surgical Treatment by Spongiosa Plombage of Juvenile Patients with Bone Cysts. H. Hellner. Chirurg 29:97-103 (March) 1958 (In German) [Berlin].

The author reports on 5 patients, between the ages of 6 and 15 years, with bone cysts occurring in the upper metaphysis of the humerus and of the femur or in the diaphysis of the humerus, who were operated on by filling the cavity in the bone with spongy substance obtained from the ventral surface of the patient's ilium. The fluid was removed from the cavity and the spongy substance introduced into it through a small opening made in the wall of the cyst with the aid of a chisel; this opening makes stripping of the connective tissue membrane possible. Excellent results were obtained. Deficient fixation, functional impairment, infection, or refracture requiring a secondary operation was not observed in any of these 5 or all the other juvenile patients with bone cysts of the humerus, femur, or tibia who in the last 6 years were operated on according to this technique. The method was also used successfully for the treatment of patients whose bone cavities did not contain fluid but fibrous giant-cell (osteoclast) tissue with small active foci of decomposition of bone. In only 1 patient the additional use of a pin was required for stabilization.

The results of plombage with spongy substance are superior to those of purely conservative treatment with an abductor plaster-of-paris dressing which is unreliable. Plombage with spongy substance is preferred to treatment by apposition of thick pieces of cortical substance or ribs. Nailing alone is not recommended. True recurrences, i. e., definite progressive decomposition of bone or a zone of transformation associated with the risk of spontaneous fracture, were not observed after plombage with spongy substance. The latter is the method of choice for the treatment of bone cysts with or without areas of giant-cell–fibrocyte tissue.

Implantation Recurrence of Carcinoma of Rectum and Colon. L. P. Le Quesne and A. D. Thomson. New England J. Med. 258:578-582 (March 20) 1958 [Boston].

Cancer cells implanted onto a raw tissue surface are capable not only of surviving there but also of growing and forming a metastatic nodule. Such recurrences have been described after operations for carcinoma of the breast, bladder, and ovary. In addition, it is now apparent that in lesions of certain hollow viscera similar implantation recurrences may occur, even though the operation has in no way transgressed the limits of the growth, as the result of the shedding of viable tumor cells into the lumen of the viscus. In particular, this complication is apt to occur after operations for carcinoma of the large intestine. The danger of this type of recurrence is exemplified by the 3 cases presented in this paper. In the first of these 3 patients a recurrence at the suture line was due to implantation of malignant cells during the original operation. In the second patient the carcinoma was at the site of the upper end of the lateral hemorrhoidectomy wound on the left. Although it was possibly a second primary growth, it was regarded as resulting from implantation of malignant cells onto the raw hemorrhoidectomy wound. This supposition was supported by the entirely superficial situation of the tumor. The third patient had a recurrence in the perineum after an abdominoperineal excision. Despite the early invasion of the perirectal fat, the initial excision appeared complete, and it seems most likely that the recurrence should be ascribed to implantation of malignant cells spilt into the wound as a result of accidental opening of the rectum close to the growth during the first operation.

Recurrence of the growth at the intestinal suture line is now a well-established hazard after operations for carcinoma of the large intestine that involve excision of a portion of the colon followed by restoration of intestinal continuity by an immediate anastomosis. It is clear also that recurrences at the suture line after restorative operations are due not to inadequate excision of the primary tumor but to implantation onto the cut edge of the intestine of viable tumor cells shed into the lumen. This desquamation of malignant cells takes place not only during handling of the growth at operation but also during the weeks and months that the tumor is present before diagnosis and treatment. Evidence of this continual shedding of viable cells is provided by the many well-authenticated cases of implantation of carcinoma of the intestine in the track of a preexisting fistula in ano. The prevention of implantation of carcinoma is discussed not only with regard to restorative operations but also with regard to the importance of not performing any operation on the distal part of the intestine until the primary tumor has been removed. The latter point is of greatest significance in relation to benign adenomas found on sigmoidoscopy distal to a carcinoma. It is wise to delay their removal until after excision of the proximal part of the malignant tumor.

Patellectomy: Repair by Quadriceps Tenoplasty. H. O. Marsh, H. O. Anderson and O. Pliego. Am. Surgeon 24:273-279 (March) 1958 [Baltimore].

Marsh and associates employ the standard anteromedial incision for their technique of patellectomy with quadriceps tenoplasty. The patella is excised by sharp dissection, preserving all healthy soft tissue, and all debris is removed from within the joint. The surgical defect is repaired with the knee in extension, plicating the capsule transversely under slight tension with mattress sutures. A triangular tongue of tendon from the superficial layer of the quadriceps tendon (that of the rectus femoris) is reflected distally. The apex of this tendon flap is 4 in. above the former patellar site, and the base is 2 in. in width. The reflected portion of the quadriceps tendon is split longitudinally into 2 equal segments in a sagittal plane. A small hemostat is forced transversely through the mid-point of the patellar tendon creating a tunnel. The reflected tendon strips are drawn through this opening from the respective medial or lateral side and sutured under moderate tension. Superficial to the patellar tendon, the tails of the tendon flaps are again crossed and sutured. The edges of the tendon donor site are approximated with interrupted sutures. After wound closure, a pressure dressing is applied to minimize postoperative swelling, but the knee is not immobilized. Quadriceps muscle exercises and active knee motion are initiated on the first postoperative day. The patient is encouraged to be as active as possible. Crutch walking is started on the 4th or 5th day and continued for 2 or 3 weeks, after which the patient is ambulatory without support.

During the past 15 years the authors employed this method of patellectomy on 36 knees in 31 patients. There were 14 knees with acute patellar fractures (including simple, complicated, and compound fractures), 9 cases of osteoarthritis, 5 patients with severe chondromalacia, 2 with nonunion or malunion, and 6 with recurrent dislocation of the patellar with degenerative joint disease. The authors were able to examine 27 knees at follow-up examinations, and information on the condition of 5 other knees was obtained by letter; the remaining 4 knees were lost to follow-up. The power in the patellectomized knee was always less than that in the knee not operated on. This decrease in strength was secondary to the loss of the patellar pulley action. Quadriceps atrophy was demonstrable in all cases. Diminution of quadriceps power and some atrophy was undoubtedly present in a number of patients preoperatively. The rapidity with which quadriceps power and good knee function was regained was directly proportional to the patient's diligence in his rehabilitation program. There was a complete range of active knee motion in 11 patients, while in the remaining 25 there was some loss. Limitation of knee motion had been anticipated preoperatively in many of these patients. The authors believe that knowledge that a patellectomy will not restore a knee to normalcy in certain disabling conditions should not deter the surgeon from its employment given the proper indications. A knee incapacitated 50% by osteoarthritis, chondromalacia, or traumatic incongruities of joint surface and restored to a 15% disability is a highly successful result. The authors list the following indications for patellectomy: (1) comminuted fractures; (2) malunited fractures; (3) nonunion; (4) advanced osteoarthritis of the patellofemoral mechanism; (5) chronic symptomatic chondromalacia; and (6) recurrent dislocation with degenerative changes.

Colloid Carcinoma of the Colon in Children. J. A. Buchman and J. D. Calhoun. Am. Surgeon 24:280-286 (March) 1958 [Baltimore].

The authors were able to collect 50 cases of proved carcinoma of the large intestine (excluding rectum and rectosigmoid) in patients 16 years of age or under. They believe that the true incidence is probably higher than this number suggests. Two illustrating case histories are described. The first was that of a 15-year-old boy in whom the roentgenologist reported a complete obstruction of the colon in the upper sigmoid area which corresponded to a palpable mass. At operation the boy was found to have a large mucoid type of carcinoma of the upper sigmoid colon with a small liver metastasis. A radical resection was done. The patient survived 6 months and died of diffuse carcinomatosis.

The second case history presented was that of a 13-year-old girl who had had vague epigastric and paraumbilical pain for 3 months. Pain was severe for 10 days, and there was nausea and vomiting for 8 days. The abdomen was opened through a McBurney incision, the incision was extended, and the diagnosis of carcinoma of the colon was established. The colon was decompressed. Ten days later a radical resection was done for a mucoid carcinoma of the splenic flexure. Twenty-six months later rectal examination revealed a movable mass in the cul-de-sac. A large Krukenberg tumor of the left ovary was removed. The patient had gross metastases to other abdominal organs, and she died 4 months later of generalized carcinomatosis.

The incidence of carcinoma of the colon was most frequent in 12-year-old children. One child was only 3 years old. Boys greatly predominated over girls (35 and 15 cases respectively). The distribution of the primary site of growth in the children studied was essentially the same as in adults. There is no explanation for the increased frequency of carcinoma in the pelvic colon, which is found both in children and in adults. In general, malignant diseases in the young are more virulent than in adults. This is also true of carcinoma of the colon. The fact that, in 20 of the 46 children in whom the lesion was examined microscopically, the diagnosis was colloid or gelatinous carcinoma indicates that the incidence of colloid carcinoma of the colon is much higher in children than in adults (46% compared with 5% or less). The treatment of carcinoma of the colon in children is the same as in adults, except that the operative procedure should be more radical in children than in adults. Most of the children reported had been treated for many months before the exact diagnosis was established. It is hoped that the unfavorable prognosis can be improved with earlier diagnosis.

Results of Surgical Treatment of Patients with Phantom Limb Pain. R. Wüllenweber. Chirurg 29:115-118 (March) 1958 (In German) [Berlin].

According to the author, surgical methods employed at the neurosurgical clinic of the University of Bonn for the treatment of phantom limb pain were based on an interruption of the pain paths between the periphery and the pain centers in the thalamus and the cerebral cortex respectively. Obliteration of the peripheral nerves by injections of alcohol was performed on 33 patients. It is the most sparing method which places the smallest load on the entire organism. Eighteen of the 33 patients obtained temporary improvement, but repeated surgical intervention became necessary later. Of 12 patients who were followed for several years, considerable improvement continued postoperatively for 2 years in 6, but only 2 were completely free of pain for more than 5 years. In 1 patient whose forearm was amputated, the phantom limb pain subsided, but the stump remained painful. Foerster's operation of cutting intradurally the thoracic nerve roots, a major operation associated with risk of injury to the spinal cord and loss of spinal fluid, was performed on 10 patients, 9 of whom had undergone various previous operations on the peripheral nerves. Follow-up examinations were performed 3 to 10 years after the Foerster operation in 9 patients, and not a single patient was completely free of pain. Postoperative improvement lasted for several weeks or months only. Sympathectomy was performed on 15 patients between 1946 and 1950: 8 of these patients were subjected to cervicothoracic sympathectomy, and 7 underwent lumbar sympathectomy. All these patients showed clinical signs of changes in the autonomic nervous system. Sympathectomy had no effect on the phantom limb pain in 3 patients. Of 13 patients who were reexamined 1 year after the operation, only 2 were free of pain. Of 12 patients who were followed for 7 to 12 years, only 1 was completely free of pain.

Unilateral (contralateral) or bilateral spinothalamic chordotomy was performed on 10 patients. Two patients were therapeutic failures, but 8 were improved by the operation and remained free of pain for 1 to 3 years after the operation. Only 1 patient remained free of pain for more than 7 years, and up to now there has been no recurrence of pain; this patient was able to resume his work as an industrial worker. Psychotherapy preceded chordotomy in 2 patients but was ineffective. Psychotherapy after chordotomy was practiced in 1 patient but resulted in only minor improvement. The reported data show that the late results of surgical treatment of phantom limb pain are poor. Consequently, more conservative methods, such as procaine hydrochloride infiltration of the peripheral cerebrospinal and sympathetic nervous system, and "pharmacological leukotomy" with phenothiazine derivatives, such as promethazine (Atosil), were performed on a larger scale with satisfactory results; however, long-continued improvement was not observed. Intensive psychotherapeutic treatment seems to be justified.

Aortography in Diagnosis of Diseases of the Thoracic Aorta. G. A. Natsvliskvili. Khirurgiya 34:92-97 (No. 1) 1958 (In Russian) [Moscow].

Aortography is a valuable method of examination in diagnosis of patency of the ductus arteriosus, anomalies, and aneurysms of the aorta. Aortography aids the surgeon in solution of problems of diagnosis and surgical tactics. The author usually practices the transcarotid approach on the left. A special catheter is introduced through an opening in the common carotid artery until the arch of the aorta. The dose of the contrast medium equals 1 ml. per kilogram of body weight. Aortography was performed on 20 patients, involving 14 with suspected patency of the ductus arteriosus, 4 with coarctation of the aorta, and 2 with aneurysms of the thoracic aorta. There were no complications after this examination.

NEUROLOGY & PSYCHIATRY

Medical Treatment in Epilepsy. H. H. Merritt. Brit. M. J. 1:666-669 (March 22) 1958 [London].

The treatment of patients with convulsive seizures is divided into 3 parts: (1) removal of any factors, organic or psychological, that may play a part in the occurrence of seizures; (2) regulation of the physical and mental hygiene; and (3) administration of anticonvulsant drugs. The objective of all anticonvulsant therapy is to establish and maintain a reservoir of drug sufficient to control the seizures without producing significant side-reactions. Since the ideal anticonvulsant is not yet available, a choice must be made from a group of drugs, one or more of which is most effective for a particular seizure type or for a particular patient. When more than 1 type of seizure is present, a combination of drugs is usually more effective than a single drug. A combination of drugs will often be necessary even for patients with a single seizure type. The majority of anticonvulsants in common usage today are derivatives of barbituric acid, hydantoin, or oxazolidinedione. Other anticonvulsants commonly used at the present time include primidone (Mysoline), which has a structure similar to that of phenobarbital, succinimide derivatives, and carbonic anhydrase inhibitors. The use of these different drugs in the therapy of all types of seizures, except petit mal, are discussed.

For the successful treatment of petit mal, it is important to distinguish this seizure from other minor seizure types. The drugs commonly used for the treatment of petit mal seizures are derivatives of oxazolidine and succinimide. These drugs are not effective against other types of seizures and are thought by some to precipitate major seizure phenomena. When petit mal coexists with other seizure types, adequate therapeutic doses of phenobarbital and phenytoin sodium are indicated as well. Failure to obtain optimal results with anticonvulsant drugs is related to failure to recognize a progressive neurological disease, particularly brain tumors, failure to use proper drugs, failure to administer proper dosage, premature withdrawal of drugs, frequent shifting of drugs, poor indoctrination of the patient in regard to the therapy, and lack of recognition of the social and economic needs of the patient. The larger number of failures are related to failure to administer the proper amount of the drug and failure to use 2 or more drugs in combination. The results of treatment in 319 cases of epilepsy were as follows: controlled, 154 (48%); improved, 118 (37%); and uncontrolled, 47 (15%). The question arises as to when it is advisable to withdraw medication. The author makes it a rule to administer anticonvulsants to patients with any type of seizure except petit mal for a period of at least 3 years after all seizures have disappeared. At this time the dose of the drug can be reduced every 4 to 6 months by one-third to one-fifth of the amount required to control the seizures. If seizures recur, the drug should be readministered in full dosage. The results obtained in the attempt to discontinue anticonvulsant therapy in patients who had been seizure-free for a prolonged period have been disappointing, except for those with petit mal attacks.

Epilepsy as a Social Problem. Lord Cohen of Birkenhead. Brit. M. J. 1:672-675 (March 22) 1958 [London].

The label "epilepsy" embraces a wide range of disability and covers fits varying widely in frequency, severity, and type. At one end of the scale there is the epileptic with a history of infrequent attacks in the past, now free from attacks or with an occasional fit at long intervals; at the other end of the scale there is the epileptic with crippling motor disabilities, including paralysis and involuntary movements, and/or severe mental changes—dementia, depression, hallucinations, confusion, and severe behavior disorders. The most pressing task is educational. The public has long believed that epilepsy is synonymous with mental deficiency and uncontrollable criminal impulses, and the epileptic is thus too often treated as a pariah. These beliefs must be dispelled. The community must learn that 80% of epileptics (including those whose epilepsy follows a brain operation or injury) can, with appropriate care and encouragement, lead a normal life. Not every fit in childhood means lifelong epilepsy; 75% of children who have had fits lose them in adult life. Experience shows that under the right conditions 80% of epileptic children can be educated in ordinary schools; about 20% need special educational facilities because of mental backwardness, behavior problems, motor disabilities, frequency of fits, incontinence of urine and feces, and postepileptic automatism. If there is doubt about the suitability of the epileptic child for an ordinary school education, a "trial" term might be given. Most special schools for epileptics are residential. This is an advantage because it provides the opportunity for continuous medical supervision.

On leaving school the epileptic should be assessed with respect to his suitability for a particular job and to jobs suitable for his particular ability and gifts. Sometimes all that is needed is advice about the hazards of occupations which must be avoided. In most cases, however, resettlement in the community demands the combined knowledge, experience, and efforts of the family physician and specialists, local welfare and health officers, employment officers, and others. The unemployed epileptic tends to become depressed, morose, apathetic, and sometimes aggressive. Work, especially if it brings economic security, provides not only an interest but instills a sense of independence and responsibility which facilitates social adjustment. Some epileptics may be given vocational training at an industrial rehabilitation unit. There remains a small residue of epileptics who cannot be placed in the open labor market. For these the alternatives are employment in a sheltered workshop, home employment, or admission to a colony.

Marriage and its physical accompaniments do not aggravate epilepsy; it is often followed by improvement. Available figures suggest that, if 1 parent is epileptic, the risk of having an epileptic child is 1 in 40. This incidence may be misleading when one attempts a prognosis in the individual case. Driving an automobile may be necessary to certain types of employment, but traffic regulations preclude anyone suffering from epilepsy from claiming a driving test. But what of the epileptic whose fits have been arrested for some time? Some physicians permit the patient to drive his own car (he must never be employed as a driver on public transport) after 3 years' freedom on treatment or 2 years without any drug therapy. This is a caluclated risk, not only for the patient but also for others. However, there are exceptions, and each case should be individually assessed.

The Results of Treatment in 1,086 General Paralytics, the Majority of Whom Were Followed for More than Five Years. R. D. Hahn, B. Webster, G. Weickhardt and others. J. Chron. Dis. 7:209-227 (March) 1958 [St. Louis].

The study presented is an evaluation of the efficacy of penicillin in 1,086 patients with dementia paralytica, who were treated in a group of clinics, including Bellevue, Boston Psychopathic, St. Elizabeth's, Grady Memorial (Emory University), Johns Hopkins, New York, University of Michigan, and University of Pennsylvania hospitals. To insure uniform coding of records at the various institutions, work sheets were drawn up, and the results were transferred to punched cards. The fixed point of reference was the "study treatment" date, that treatment episode which placed the patient in the study group whether previous treatment had been given elsewhere. Patients were observed at 3, 6, and 12 months after study treatment and yearly thereafter. Of the 1,086 patients, 629 were treated with penicillin alone, and 457 with penicillin plus fever therapy, usually induced tertian malaria. The usual incubation period of dementia paralytica was 10 to 24 years after syphilitic infection. The simple dementing type of psychosis was more frequent than all other types combined. In the absence of previous treatment, the spinal fluid complement fixation reaction was always positive, and the spinal fluid cell count was almost always elevated.

None of the 1,086 patients had received penicillin for early syphilis. Paresis was not observed after penicillin treatment of asymptomatic neurosyphilis. Additive effects of fever therapy were not sufficient to justify its use. Early diagnosis and prompt penicillin treatment of incipient parasis resulted in clinical remission and ability to work in more than 80% of the patients; this treatment will prevent practically all deaths from neurosyphilis, and even the institutionalized patient has 1 chance out of 3 of improvement and rehabilitation. In contrast to the dire prognosis of untreated paresis (death within 4 years), only 9% of penicillin-treated paretics were dead of paresis 10 years after treatment. Even so, the penicillin-treated paretic patient had nearly 4 times the death rate of his or her nonsyphilitic age, race, or sex counterpart. While some symptoms of paresis were favorably influenced, abnormalities of speech, insight, calculation, judgment, and general information did not entirely disappear. Repository penicillin was as suitable as aqueous penicillin. Although the minimal effective dose is unknown, this study suggested that 6 million units is probably ample.

In general, more than 1 course of penicillin was of no demonstrable additional value. The Herxheimer reactions, notably exacerbation of the paretic pychosis or convulsive seizures, occurred more frequently in the presence of spinal fluid pleocytosis than in its absence. The Herxheimer reaction did not cause long-term damage. Posttreatment psychiatric hospitalization was directly proportional, and clinical improvement and rehabilitation for work were inversely proportional, to the severity of pretreatment psychosis. The presence at the time of treatment of incontinence, of inability to perform simple acts of personal toilet, and of convulsions afforded a particularly poor prognosis for longevity. Work status was of great prognostic import, and so was the time that had elapsed since the patient had been able to work at his usual occupation. Pretreatment pleocytosis indicated an active process amenable to treatment, but in some patients it left behind sufficient brain damage to nullify any clinical effect. The absence of pleocytosis indicated a relatively static process less susceptible of improvement. Clinical progression occurred more frequently with persistent cerebrospinal fluid cell counts of 5 to 10 per cubic millimeter than with cell counts of 4 or less. Considering that with the decreasing incidence of syphilis dementia paralytica is becoming a neuropsychiatric rarity, the authors note that these data are perhaps of more historical interest than practical importance.

PEDIATRICS

Exchange Transfusions: Experiences at University of Kansas Medical Center Over a Two-Year Period. D. S. Overend. J. Kansas M. Soc. 59:83-89 (March) 1958 [Topeka].

The author reports on 46 exchange transfusions performed on 43 infants. The conditions for which transfusion was required included hemolytic disease of the newborn due to fetomaternal incompatibility of the Rh factor or of the ABO blood groups and, in some cases, hyperbilirubinemia without demonstrable incompatibility, hereafter referred to as idiopathic hyperbilirubinemia. Rh incompatibility was demonstrable in 19 patients (44%), ABO incompatibility in 12 patients (28%), and idiopathic hyperbilirubinemia in 12 patients (28%). The incidence of prematurity was greater in idiopathic hyperbilirubinemia than in the other types of hyperbilirubinemia; 4 of 12 infants with idiopathic hyperbilirubinemia weighed less than 2,500 Gm. (5½ lb.) at birth. In the Rh group, 2 of the 19 infants were premature, while in the ABO group, only 1 of the 12 was premature.

Infants receiving exchange transfusion during the first 24 hours of life can usually be cannulated through the umbilical vein; those receiving exchange transfusions later, after the umbilical cord is no longer usable, are cannulated through the greater saphenous or the common femoral vein. Blood is withdrawn and administered in 20-ml. increments, except in the case of very ill or premature infants, when 10-ml. increments are used. At the completion of each 100 ml., 1.0 to 1.5 ml. of 10% calcium gluconate is administered through the canula. In very small infants, 1.5 ml. of calcium gluconate is given after each 50 ml. of exchange. The calcium gluconate should be given cautiously, and the apical pulse should be constantly checked while it is given. Marked bradycardia is an indication for slowing or discontinuing the administration of calcium gluconate. Throughout the transfusion the infant is carefully observed for cyanosis, for excessive irritability which may indicate impending tetany, and for vomiting. Oxygen is administered by face mask throughout the procedure. The infant is returned to the nursery immediately after the exchange transfusion and is kept in a heated crib for 2 to 4 hours. Feeding is withheld for 4 to 8 hours depending on the condition of the infant. Antibiotics are given routinely for 48 hours after the transfusions.

Four patients in the series expired; 3 of these were referred late from other hospitals when evidence of brain damage was already present. The 4th fatality occurred at 52 hours of age after exchange transfusion at 6 hours of age; death was the result of hyaline membrane disease complicated by marked emphysema and pneumothorax. No permanent sequelae occurred in infants given exchange transfusions before the concentration of indirect bilirubin in the serum reached 15.0 mg. per 100 ml. Cannulation of the femoral or saphenous veins is often followed by cyanosis and edema of the limb, but in no case did cyanosis and edema persist for more than 48 hours. No permanent undesirable sequelae were observed in any patient after cannulation of the femoral or saphenous veins.

The presence of hydrops fetalis is an indication for immediate emergency exchange transfusion; otherwise, the decision is based on hyperbilirubinemia according to the following rules: (1) a serum indirect bilirubin level rising at a rate exceeding 0.5 mg. per 100 ml. per hour in the first 24 hours of life or exceeding 10 mg. per 100 ml. in the first 24 hours; (2) a rising indirect bilirubin approaching 20 mg. per 100 ml. at any time in the neonatal period; a lower minimum value (16-18 mg. per 100 ml.) is employed in premature infants; (3) inability of the laboratory to demonstrate blood group incompatibility does not alter the decision to perform an exchange transfusion if the indirect bilirubin reaches levels meeting either of the above criteria. Bilirubin determinations may have to be made as often as every 6 hours until the rate of rise of bilirubin concentration is established or as infrequently as every 24 hours in some patients, especially those with idiopathic hyperbilirubinemia. Studies of infants with hyperbilirubinemia have been greatly simplified by the adoption of "microbilirubin" determinations, in which the bilirubin concentration is estimated in specimens obtained by heel puncture.

The Superficial Inguinal Pouch and the Undescended Testis. P. Jones. M. J. Australia. 1:239-242 (Feb. 22) 1958 [Sidney].

The superficial inguinal pouch is an areolar space lying beneath Scarpa's fascia and in front of the external oblique aponeurosis. It is oval in outline and directed obliquely upward and laterally from the pubic tubercle. This pouch has been called the "abdominal scrotum" and varies in size. The wide range of mobility of the testis in childhood is well known, and the brisk cremasteric reflex will often retract the testis out of the scrotum. When its withdrawal is traced by palpation, it is found to have entered an extensive space situated within the fascia of the anterior abdominal wall—the superficial inguinal pouch. Such a testis is described as a "retractile testis," and while this is a convenient clinical term for a variety of normal testes, it is scarcely justifiable, as all testes in prepubertal boys are of this type. As the testis becomes larger and heavier during puberty and the cremasteric reflex becomes less brisk, the testis comes to reside permanently in the scrotum. The size of the testis prevents its passage into the superficial inguinal pouch. This constitutes the usual adult anatomy, but occasionally a fascial ring larger than the testis persists, with the same clinical findings as in childhood.

The retractile testis has probably accounted for many of the successes claimed for hormone therapy in "undescended testis." Equally important is the possibility of misinterpretation of the clinical findings when a normal testis is palpable in the superficial inguinal pouch. Finger-tip manipulation will bring the testis into the scrotum, and, if this maneuver is omitted, the testis may be misdiagnosed as "undescended." There are 2 main categories of undescended testes—those arrested in the line of normal descent and those that have diverged from it. The latter are known as "ectopic testes," and 4 types are described: superficial inguinal, perineal, femoral, and penile. The superficial inguinal ectopic testis is the commonest variety, and the anatomic basis of this type is an abnormality in the attachment of Scarpa's fascia. The clinical characteristics of a superficial inguinal ectopic testis are as follows: The testis is of normal size, widely mobile within the pouch, and when it is manipulated toward the scrotum it reaches the level of the pubic tubercle and is then directed forward by the concave upper surface of the obstruction. Such a testis can never spontaneously descend into the scrotum. After commenting on uncommon variants of this type of ectopic testis, the author discusses the differentiation of a normal retractile testis from a superficial inguinal ectopic testis by the fact that there is a free communication between the pouch and the scrotum in the former which is absent in the latter. A knowledge of the normal and the abnormal anatomy is essential for accurate clinical diagnosis.

Congenital Toxoplasmosis. R. D. Montgomery, B. Donnison and H. Jolly. J. Clin. Path. 11:114-118 (March) 1958 [London].

Hydrocephalus, choroidoretinitis, convulsions, and intracerebral calcification are the 4 characteristic manifestations of congenital toxoplasmosis, but it is probable that the disease may still pass unrecognized as a cause of obscure oculocerebral defect or perinatal death. Two cases are reported. The first infant died 22 days after birth, and autopsy revealed intracellular and free forms of Toxoplasma organisms in the brain tissue. This case illustrates the remarkable pathological changes that may be found in the acute infection. The second child was spastic and microcephalic from birth. He refused to suck and developed severe ulcerative stomatitis on the third day, associated with a discharge from both eyes. When 4 weeks old, he had a series of convulsions, which persisted for a week, and thereafter remained spastic, with frequent jerks and occasional convulsions. On admission to hospital at the age of 9 months, he was found to be a microcephalic idiot, with marked microphthalmos, a small snuffy nose, and large ears. All the limbs were spastic, with flexion of the arms and hands, extension of the legs, and frequent jerking movements of the whole body. Death occurred 4 days after admission.

There is no positive evidence that the second child's condition was due to toxoplasmosis, although, if this were the case, it would represent an early burnt-out infection in which, with negative serology, one would not expect to find surviving organisms. The mother showed evidence of recent infection with Toxoplasma organisms. The mode and significance of maternal infection are discussed. Although it appears that the possible paths of infection are multiple, there is some evidence in favor of the oropharyngeal route. The only manifestation likely to give rise to the diagnosis in pregnancy is the glandular syndrome. Transplacental transmission has only been shown to occur as a result of infection acquired during pregnancy, and even in this event the degree of hazard to the fetus cannot at present be assessed. The importance of toxoplasmosis in relation to mental deficiency, microcephaly, and ocular defects may be greater than is revealed by current diagnostic criteria. The absence of serum antibodies after the first few months of life does not exclude a past infection in utero.

OTOLARYNGOLOGY

Possibilities and Results of Tympanoplasty on the Basis of 400 Operations. R. Maspétiol. Semaine hôp. Paris 34:595-598 (Feb. 26) 1958 (In French) [Paris].

Tympanoplasty is used in chronic otitis and its sequels, (1) as a reparative operation for the reconstruction of the tympanum with a skin graft and (2) as a functional procedure designed to restore the best possible auditory capacity to the ear. The successful creation of a new mobile tympanum is essential to, but not always sufficient for, the restoration of hearing. It is useless, for instance, to expect functional improvement in patients in whom a decided loss in osseous conduction bears witness to involvement of the labyrinth. Tympanoplasty in such cases can only be used as a reparative procedure, chiefly for the purpose of suppressing discharges of tubal origin. The auditory gain to be expected from the operation will depend on the preoperative audiometric curve and the extent of the anatomic lesions. An intact ossicular chain provides hope for either excellent or subnormal hearing if bone conduction is preserved, but when the ossicular chain has been destroyed, a threshold of 25 to 30 db. is the most that can be expected. Patients with a preoperative threshold of 30 db. cannot expect any elevation of this threshold after closure of the perforation in the tympanum. The audiometric curves are sometimes abnormally good in relation to the anatomic lesions because of adhesions between an isolated stirrup, for example, and either the handle of the hammer or the vertical branch of a partially destroyed anvil. Adhesions of this kind, which play a part in the transmission of sound and which are physiologically effective, should be carefully preserved, because their inadvertent severance may have an adverse effect on the hearing. Medical treatment designed to suppress infection and to improve the general condition should always be given before tympanoplasty is undertaken in patients of any age with quiescent chronic otitis or otorrhea of tubal origin, or in children.

The present possibilities of tympanoplasty are shown by the results obtained in 100 patients with a postoperative follow-up of at least 3 months. The first 300 such operations in the author's series are not considered, because increasing experience has enabled him to obtain better results in the later cases. The indications for operation were cicatricial otitis in 48 cases and suppurative otitis in the other 52. A new mobile tympanum, with a freely aerated eardrum behind it, was obtained in 45 of the 48 patients with cicatricial otitis. This anatomic reconstruction was accompanied by an improvement in hearing in 36 of the 39 patients in whom the ossicular chain was intact and in 5 of the 7 in whom it was broken. The results were, on the whole, less satisfactory in the cases of suppurative otitis, because suppuration threatens the vitality of the graft and favors the formation of adhesions which may interfere with any postoperative improvement in hearing. Even so, an anatomic reconstruction was obtained in 37 of the 52 patients, and the hearing was improved in 4 of 6 patients with an intact ossicular chain and in 24 of the 31 in whom the chain was broken. These results warrant the conclusion that tympanoplasty is the operation of choice in chronic suppurative otitis and its sequels.

Olfactory Sensation Stimulated by Intravenously Administered Substance. C. Semeria. Arch. ital. otol. 68:9-78 (Dec. [Supp. 30]) 1957 (In Italian) [Milan, Italy].

The author made a psychophysiological study, which he believes to be the first recorded, of the olfactory sensation stimulated by intravenously administered substance in various groups of persons, some of them with a modal and the others with a deviant sense of smell. Threshold concentration values stimulated by intravenously administered peppermint were observed in a group of 83 persons with a modal sense of smell. In 52 (62.6%) of the subjects, the threshold of stimulation was reached by 2.5 mg. of peppermint (Mentha piperita), but on occasion quantities as high as 5 mg. or 7.5 mg. were required. Two persons did not perceive the presence of peppermint through the olfactory but only through the palatal apparatus. The mean value of threshold concentration values thus oscillated around 3 mg. of intravenously administered peppermint in 92% of the persons in this series. The thresholds were lowest at fasting state in the morning and highest at satiated state and in tired persons. The lapse of time from the moment of intravenous administration in the arm until the onset of olfactory sensation varied between a minimum of 7 to 8 seconds (in 29 persons) and a maximum of 25 seconds (in 4 persons).

Adaptation of the olfactory nerve stimulated by intravenously administered substance was observed in 39 persons with low threshold concentration values. No adaptation of the olfactory nerve was noted in 30 persons, a mild adaptation in 5, and a distinct adaptation in 4. The pupillary activity associated with the olfactory sensation was observed in 19 of 20 persons who received the intravenously administered substance. There is an immediate pupillary contraction lasting 0.5 second, followed by a mydriasis lasting from 0.5 to 1 second. The psychogalvanic reflex was observed in 14 of 16 young persons taking the test. Recordings of the olfactometric test by Elsberg showed response to intravenously administered substance in most laryngectomized persons. Threshold concentration values appeared higher in patients who had undergone laryngectomy at a more remote date than in those who had had the operation recently.

The same test was given to 322 persons with various clinical disorders; 252 of them had various types of rhinosinusal disorders, 27 had neurological disturbances, and 43 had cranial lesions. Persons with simple nasal obstruction, chronic rhinosinusal inflammations, and allergic rhinal disorders showed higher than normal threshold concentration values. There was no observed olfactory sensation stimulated by intravenously administered substance in persons with postrhinitic olfactory alterations. Inconsistent results were obtained in persons with ozena. Almost identical findings of the olfactory response to intravenously administered substance were obtained through various olfactometric procedures in persons with neurological disorders and cranial lesions.

INDUSTRIAL MEDICINE

Chronic Beryllium Poisoning. J. W. Jordan and C. S. Darke. Thorax 13:69-73 (March) 1958 [London].

The authors describe the history of a woman who was first seen in 1955 when she was 45 years old. She had chronic cough and clubbing of the fingers. Her occupational history revealed that from June, 1943, to May, 1945, she had worked in a factory making fluorescent lamps. At the time, zinc beryllium silicate phosphors in high concentration were used in the manufacture of these lamps. The patient's work consisted in placing the tubes on horizontal rollers. The solution containing beryllium was baked on the inner surface of the tubes, and after the tubes were removed from the oven, about 2 in. of deposit was extracted from each end of the tube with a rubber-padded brush. Very little dust was released, as the ends of the tube were enclosed in a box covering. Tubes were broken from time to time, and the patient received some small lacerations from these. During this period she felt quite well, and no medical or radiologic examination was made.

In 1945 the patient went to live in a small town far removed from that in which she did her factory work. A few years later a gradual deterioration in her health was noticeable, and she found that she was unable to take long walks because of shortness of breath. In 1950 an unproductive cough and vague chest pains developed, and clubbing of the fingers was first observed by the patient. During the next 5 years the cough became more severe. The patient sought medical advice, and a diagnosis of chronic beryllium poisoning was made 10 years after her last exposure. She was found to have moderate respiratory insufficiency, radiographic evidence of a diffuse granulomatous and fibrotic process in the lungs, splenomegaly, and a number of sarcoid-like granulomas on the forearm, knees, and ankles. Her skin gave a strongly positive reaction to a patch test with a dilute solution of beryllium salt. The observation that all patients with chronic beryllium poisoning show positive patch tests is thought to support the view that the development of a hypersensitive state is an essential feature in the pathogenesis of the disease.

Occupational Eczema in Shoemakers Resulting from Use of a New Type of Glue. K. E. Malten. Nederl. tijdschr. geneesk. 102:268-272 (Feb. 8) 1958 (In Dutch) [Amsterdam].

Weeks or months after the introduction of a new type of glue, contact eczema developed on the hands and forearms of a number of shoemakers. The phenolformaldehyde synthetic resin contained in the glue was found to be the causal allergen by means of patch tests on 10 of the affected workers. The resin consisted of a catalyst of unknown composition, of formaldehyde, and of *p*-tertiary butyl phenol. Two patients had positive patch tests for formaldehyde; all 10 patients were allergic to *p*-tertiary butyl phenol, and so this was probably the primary sensitizing agent. The case histories revealed that the same or a closely related resin was a component part of various other glues. No new cases of this industrial dermatitis need occur, provided that certain precautions are taken. Preventive measures are listed.

THERAPEUTICS

Treatment of Certain Side-Effects of Morphine. G. Christie, S. Gershon, R. Gray and others. Brit. M. J. 1:675-680 (March 22) 1958 [London].

Three drugs are necessary for the complete control of the side-effects resulting from the administration of morphine, namely, N-allylnormorphine for respiratory depression, amiphenazole for central nervous system depression (narcosis), and cyclizine hydrochloride for nausea and vomiting. Experiments and some case histories are presented to illustrate the 3 major therapeutic exhibitions of morphine: 1. Patients with incurable painful disease, in whom some degree of habituation is soon established and the incidence and severity of side-effects fall off. 2. Preoperative and postoperative patients. This group comprises a wide range of persons with respect to age and physical conditions; the postoperative group is a particularly important one, as nausea, dry retching, and vomiting can cause serious surgical sequelae. 3. Accident casualties and war-wounded in whom morphine is used as an emergency analgesic. It seemed desirable at the outset to establish the incidence and severity of the side-effects of doses of the order of 15 to 30 mg. Morphine was given by injection, usually intramuscularly but occasionally intravenously.

Summarizing their observations, the authors emphasize that the most frequent side-effects are nausea and vomiting, the incidence of which may be as high as 30%. The only really effective drug to control morphine-induced emesis is a mild antihistaminic, cyclizine hydrochloride. On the other hand, the narcotic (sedative) action of morphine is best controlled by amiphenazole. These 2 results, in man, parallel the results obtained in animals. There is also some evidence that amiphenazole can aid in the relief of morphine addiction. N-allylnormorphine would appear to be the drug of choice to restore a morphine-depressed respiratory center, although amiphenazole has some action in this regard. Morphine, in healthy people, is not the dangerous drug that has hitherto been believed. However, certain patients are susceptible to morphine. Thus, in the first series 6 out of 48 volunteers were sensitive to 10 mg. of morphine, but even in this group respiratory depression was not the major concern. It is advisable to ascertain this sensitivity by giving the conventional dose of 10 to 15 mg. If this amount is without untoward effect, then the dose of morphine should be rapidly increased to 30 mg. or more until the patient receives complete analgesia lasting 6 to 8 hours. Large doses of morphine (up to 200 mg. daily) may be required to control chronic pain. The patient should not be denied the benefit of complete analgesia on the score of side-actions or addiction. The results in over 400 cases show such fears to be groundless when the appropriate antagonist is employed to control the particular side-action experienced by the patient.

The Effect of Repeated Increased Doses of BCG Vaccine on the Organism of Infants. A. A. Efimova. Pediatriya 36:14-23 (Jan.) 1958 (In Russian) [Moscow].

De Assis and his co-workers in Brazil called attention to the desensitizing effect of large doses of BCG vaccine given at short intervals by the oral route. The author reports on oral vaccination of 317 children, aged from 1 month to 3 years. BCG vaccine in doses of 60 mg. was given every month for 6 doses to children who were either tuberculin negative or tuberculin positive. There were no complications, and no injurious effect upon the organism of the vaccinated child was noted. The method can be carried out along with other prophylactic vaccinations. The intensity of tuberculin allergy was observed to increase with each repeated vaccination so as to reach almost 100% at the end of the treatment. For practical purposes 2 to 3 vaccinations should suffice. Vaccination of children infected with tuberculosis is inadvisable.

PATHOLOGY

Effects of Linolenic and Stearic Acids on Cholesterol-Induced Lipoid Deposition in Human Aortic Cells in Tissue-Culture. D. D. Rutstein, E. F. Ingenito, J. M. Craig and M. Martinelli. Lancet 1:545-552 (March 15) 1958 [London].

A chance observation led to the study of factors affecting lipid deposition in tissue cultures of cells from the human aorta. The effects of steroids, such as cortisone, on sodium and potassium exchange between the medium and human heart cells in tissue culture were under study. Cholesterol, a steroid without known direct effect on sodium and potassium exchange, was added to one of the control cultures. After 8 days' growth cells exposed to cholesterol were found to contain granules which stained with scarlet red and with Liebermann-Burchard reagents. This observation led the authors to make studies on the deposition of lipid in tissue cultures of human aortic lining in a medium containing human blood serum. Factors affecting the intracellular deposition of lipid could be investigated by this method. It was demonstrated that, when cholesterol in ethanol is added to the culture medium, the amount of lipid deposited in the cells is proportional to the amount of cholesterol added: 1. When cholesterol was added at a concentration of 1 mg. per 100 ml., there was little evidence of intracellular lipid deposition. 2. At a concentration of 3 mg. per 100 ml., intracellular lipid deposition regularly appeared and was associated with an increase in the size of the cells. 3. At a concentration of 5 mg. per 100 ml., intracellular lipid deposition was considerable, and the cells were enormously increased in size.

Similarly, when cholesterol bound to beta lipoprotein was added to the culture medium, the amount of lipid deposited in the cells was proportional to the amount of cholesterol added: 1. At a concentration of 30 mg. of added cholesterol per 100 ml., there was little evidence of intracellular lipid deposition. 2. At a concentration of 50 mg. per 100 ml., intracellular lipid deposition regularly appeared and was associated with an increase in the size of the cells. 3. At a concentration of 70 mg. per 100 ml., intracellular lipid deposition was considerable, and the cells were enormously increased in size. The intracellular deposition caused by adding cholesterol (whether in ethanol or protein-bound) disappeared in 5 days if the medium containing the cholesterol was replaced by a normal medium. The intracellular deposition caused by adding cholesterol (whether in ethanol or protein-bound) was completely inhibited by the simultaneous addition of linolenic acid (1 mg. per 100 ml.). It was increased by the simultaneous addition of stearic acid (1 mg. per 100 ml.). Thus, in tissue cultures of human aortic cells, deposition of lipid can be induced by cholesterol, is reversible, can be inhibited by an unsaturated fatty acid (linolenic acid), and can be potentiated by the corresponding saturated fatty acid (stearic acid).

The Natural History of Postnecrotic Cirrhosis: A Study of 221 Autopsy Cases. R. A. MacDonald and G. K. Mallory. Am. J. Med. 24:334-357 (March) 1958 [New York].

In an attempt to study the natural history of postnecrotic cirrhosis, the authors analyzed the clinical, laboratory, and pathological features of 130 men and 91 women with this disease, whose average age was 57 years, who died, and in whom autopsies were performed at the Mallory Institute of Pathology in Boston between 1917 and 1956. Of the 221 patients, 31 had primary hepatic carcinoma in addition to postnecrotic cirrhosis, 26 had fatty nutritional (alcoholic) cirrhosis in addition to postnecrotic cirrhosis, and 164 had uncomplicated postnecrotic cirrhosis. Information related to previous hepatitis or jaundice was available from the clinical records of 190 patients, 45 (24%) of whom had had jaundice or an illness suggesting hepatitis. No evidence was found, however, that a sudden and massive liver insult had occurred in these patients. An additional 84 patients (44%) had been exposed to greater than usual risk from serum hepatitis in the course of receiving antisyphilitic and other parenteral injections in the course of previous surgical procedures. The clinical records of the patients with postnecrotic cirrhosis at autopsy, who had a history of previous jaundice (presumably viral hepatitis), showed 2 types of clinical course after the episode of jaundice. Sixty-six per cent of these patients had been relatively well for an average period of 15 years, after which time ascites, jaundice, or right upper quadrant pain had occurred. From the time of appearance of these features the duration of life was only 2 months. The other type of clinical course was observed in about 33% of the patients, in whom the interval from jaundice to the occurrence of ascites, recurring jaundice, or right upper quadrant pain was less than 1 year, and the length of survival, once these signs appeared, averaged only 17 months.

The average duration of continuous illness before hospitalization was less than 6 months in more than 50% of the 221 patients with postnecrotic cirrhosis. Only about 20% of the patients had been continuously ill for more than 2 years. After admission to hospital the average duration of life was 22 days. The presenting complaints of the patients were chiefly ascites and edema (30%), abdominal pain (17%), and hematemesis (14%). Abdominal pain was particularly frequent among patients with hepatic carcinoma. Such features as age and sex of the patients in this study did not differ greatly from those of other patients with cirrhosis or from the general autopsy population of the Mallory Institute of Pathology. A racial difference was noted in that postnecrotic cirrhosis was relatively frequent among Chinese, although the number of Chinese patients was small. About 50% of the 221 patients had consumed alcoholic beverages to excess; the other 50% drank little or no alcohol. An adequate diet was claimed by about 66% of the patients. Poor nutrition and alcoholism were common in patients who had fatty nutritional (alcoholic) cirrhosis in addition to postnecrotic cirrhosis. Results of laboratory and liver function tests were characteristic of patients with cirrhosis, but no specific alterations for postnecrotic cirrhosis were found.

At autopsy, the liver tended to be smaller than normal, 76% of the livers weighing less than 1,500 Gm.; the color of the liver was most frequently gray to yellow, and nodules of liver tissue tended to be large and irregular, generally greater than 2 cm. in diameter, and separated by broad fibrous scars; but the occurrence of large hepatic nodules was not an invariable finding. The spleen tended to be enlarged at autopsy, with average weights between 350 and 400 Gm. A palpable spleen was not of help in determining the presence or absence of hepatic carcinoma or esophageal varices. Bloody ascites was found in 23% of the patients with hepatic carcinoma as compared with an incidence of only 2.5% among patients with uncomplicated postnecrotic cirrhosis. Esophageal varices were found at autopsy in 52% of the patients with postnecrotic cirrhosis; 50% of these showed evidence of active, recent bleeding. The principal causes of death among the patients with postnecrotic cirrhosis were infection (29%) and gastrointestinal bleeding (26%), the latter usually from esophageal varices. Gastric and duodenal ulcers were found in 9% of the patients with postnecrotic cirrhosis, compared with an incidence of 5.5% in all autopsies at this institute, a difference that is not statistically significant. However, 16% of the patients with concurrent hepatic carcinoma had peptic ulcer. Nonhepatic neoplasms were found in 27 (12%) of the 221 patients; metastases to the liver in patients with postnecrotic cirrhosis appeared to be of the same order of frequency as in patients without cirrhosis. The authors' findings in the 221 patients leave little doubt that postnecrotic cirrhosis is both clinically and anatomically a true cirrhosis.

Unsuspected Healed Myocardial Infarction in Patients Dying in a General Hospital. S. E. Gould and L. P. Cawley. A. M. A. Arch. Int. Med. 101:524-527 (March) 1958 [Chicago].

In order to ascertain the frequency of unsuspected healed myocardial infarction, the authors reviewed a series of 5,000 consecutive autopsies and the clinical records of all patients who were found to have infarcts at autopsy. The total number of hearts with infarcts, whether old, recent, or fresh, was 588 (11.76%). The ratio of men to women with infarcts among those who came to autopsy was 1.13:1; the ratio of white to Negro patients was 2.13:1. Healed unsuspected (old, "silent") infarcts were found in 175 patients (3.5%) of all who came to autopsy and constituted 30% of all myocardial infarcts encountered at autopsy. The majority of the 175 patients with unsuspected healed infarcts (53.7%) were 70 years or older, and only 1 was less than 50 years old. Those who had congestive heart failure had associated hypertension, and particularly cardiac hypertrophy, more often than patients who did not have congestive failure. Electrocardiograms were taken in only 56 of the 175 patients with old unsuspected infarcts. In 33 the tracing was abnormal but not diagnostic of infarction.

Histological Findings in the Parametrial Lymph Nodes in Carcinoma of the Cervix. I. Priola. Minerva ginec. 9:1017-1025 (Dec. 31) 1957 (In Italian) [Turin, Italy].

The author describes microscopic findings of the lymph nodes of the parametria excised from 37 patients with carcinoma of the cervix, on whom panhysterectomy of the Wertheim type was performed during the period from 1949 to 1950. This series of patients fell into the United Nations classifications 1 and 2. Patients with the type 2 tumor had received radium therapy before the operation.

This study revealed an early carcinomatous and metastatic invasion of the parametrial area. Presence of extensive tumor infiltration into the lymph nodes was established even in cases which could have been clinically classified as tumors of type 1. Preoperative radium therapy healed the ulcerations and reduced the parametrial infiltration, thus permitting surgical operation. Histological findings, however, revealed the existence of a considerable extent of metastases, which suggest that radium therapy was not able to reach the malignant cells seated deeply in the tissue. No signs of endometriosis and only a few degenerative lesions were seen. Tumor cells, except for the area in process of degeneration, showed structural differentiation with the characteristics of the primary carcinoma. Changes in the parenchyma of the lymph nodes were of secondary importance as compared with the metastatic process. Endothelial and follicular hyperplasias were probably defensive reactions against the tumor and its necrotic products. The high incidence of carcinoma metastases has indicated the rapidity of the progress of carcinoma of the cervix.

The opinion of the author is that irradiation could not reach the lymph nodes of the parametria. Resistance of the metastatic cells to radium therapy must be ruled out, because the original tumor had regressed when exposed to irradiation. Surgical therapy thus appears to be the best procedure for management of carcinoma of the cervix of type 1 and 2. Radium therapy is useful in preparation for the surgical operation.

A Genetic Study of Carcinoma of the Large Intestine. C. M. Woolf. Am. J. Human Genet. 10:42-47 (March) 1958 [Baltimore].

It has been established that multiple polyposis is a genetic disease, with a dominant mode of inheritance. Even though multiple polyposis is a rare disease, the occurrence of a single polyp or a few polyps (occasional discrete polyps) in the colon or the rectum is a relatively common condition, routine sigmoidoscopic examinations having shown that approximately 5% of all individuals over 35 years of age have one or more polyps in the rectum or the sigmoid. Multiple polyposis is easily distinguished from the latter condition. It is a matter of hundreds or even thousands of polyps versus one or a few. There has been evidence that even the occurrence of occasional discrete polyps may be influenced by a genetic background. Fifty-five adult members belonging to the same generation of a large Utah kindred with a high frequency of carcinoma of the large intestine were given sigmoidoscopic examination. Twenty-five were shown to have 1 or more histologically confirmed polyps. This is a much higher frequency than is expected in the general population. As a further control, 21 of the spouses of these persons were examined; only 1 had a questionable polyp, and all the others were free from polyps. Twelve to 18 months after the initial examination, more than half of the persons who had polyps at the first sigmoidoscopic examination were shown to have 1 or more new polyps, and some who had been free at the first examination now had 1 or more polyps.

Since these observations suggested that carcinoma of the large intestine could have a familial tendency due to a genetic mechanism other than that associated with multiple polyposis, a propositus study was carried out. The objective was to compare the frequency of deaths due to carcinoma of the large intestine and to other types of cancer among the relatives of individuals who died of cancer of the large intestine not associated with multiple polyposis with the frequency in a control sample. Propositi were picked from death certificates between 1931 and 1951. The names of those who died of cancer of the large intestine were traced in the genealogical archives of Salt Lake City. Family group records were available for about one-fourth of the selected names, and it was then possible to trace the death certificates of parents and siblings. The death certificates of 763 relatives of the propositi revealed 26 in whom death had been due to cancer of the large intestine, whereas only 8 such deaths were found in the relatives of controls. This difference seems the more noteworthy when it is considered that deaths from other types of cancer were practically the same in the two groups, 81 and 83 respectively. Even though the number of deaths among the relatives of the propositi is significantly greater than the number among those of the controls, it is not large enough to suggest that heredity is of greater etiological importance than some other unknown nongenetic factors. The genetic component appears to have about the same magnitude of importance as has been shown for carcinoma of the stomach and breast.

ANESTHESIA

Deaths Associated with Anaesthesia and Surgery: A Critical Analysis of 200 Cases. O. V. S. Kok. South African M. J. 32:180-186 (Feb. 15) 1958 [Cape Town].

In 1955 the South African Society of Anesthetists appointed a subcommittee to investigate deaths associated with anesthesia. The present communication is concerned with reports on the first 200 such deaths during the last 2 years. It deals only with surgical deaths referred to a district surgeon for autopsy in terms of section 86 of the Medical, Dental, and Pharmacy Act of 1928, which is concerned "with the death of a person whilst under the influence of a general or local anesthetic, or in which the administration of an anesthetic has been a contributory cause." This report classifies deaths associated with anesthesia and surgery along the lines adopted by a committee in Great Britain, as follows: (1) deaths caused by the anesthetic agent or the technique of administration or in other ways coming entirely within the anesthetist's province; (2) similar cases, but in which there was some doubt whether the agent or the technique was entirely responsible for the fatal result; (3) cases in which the patient's death was caused by both the surgical and the anesthetic techniques; (4) deaths entirely referable to the surgical technique; (5) inevitable deaths, but in which the anesthetic and surgical techniques seemed satisfactory; (6) fortuitous deaths, e. g., those due to pulmonary embolism; and (7 and 8) cases that could not be assessed despite data or on account of inadequate data.

In the present analysis, 89 deaths (44.5%) fell into the first 3 categories (those in which the anesthetic played a major role). All age groups were represented in the 200 patients. As regards sex, there were 120 men and 80 women. The greater number of deaths in men was ascribed to a high relative incidence of serious trauma. As regards the stage of anesthesia at which death occurred, it is stated that 25 deaths occurred during induction, 88 during maintenance, 40 within 30 minutes after the operation, and 47 later. The preoperative status was good in 20 of the patients, fair in 40, poor in 84, and 56 of the patients were moribund. Cardiac arrest occurred on the operating table in 132 of the patients. Cardiac massage had been used in only 82 of the 132 patients. The author feels that the only effective treatment of cardiac arrest is immediate thoracotomy and cardiac massage, followed by defibrillation if necessary. The anesthetist must institute artificial respiration. Blind intracardiac injection of vasopressor drugs is criticized. Thiopentone (Pentothal) sodium was used for induction in 116 of 182 patients who were given general anesthesia. Of this number, 22 succumbed from primary cardiac failure. Thiopentone sodium was the most dangerous anesthetic agent. The death rate from trichloroethylene (Trilene) appears to be the highest of all the inhalation agents. There are peculiar dangers in the use of some agents for regional and topical analgesia.

The author recommends that anesthetic recovery rooms should be provided in which poor-risk patients can be nursed by experienced nurses under the eye of anesthetists and surgeons. Hospitals should also keep proper resuscitative equipment (cardiac massage drums, suction apparatus, etc.) immediately available. Departments of anesthesia should be established in all medical schools with status equal to that of other departments. Before registration as a medical practitioner, the intern should receive at least 1-month, full-time, compulsory training in anesthesiology, or he should give under supervision at least 100 anesthetics. Large hospitals should have committees to investigate anesthetic deaths. There should be compulsory notification of all deaths resulting from anesthesia, compulsory instruction in methods of cardiac resuscitation, and refresher courses for general practitioners, nurses, and other persons interested in modern methods of anesthesia.

The Effect of Hypothermia on Hemorrhagic Shock. A. T. Ferguson, J. N. Wilson, D. Jenkins and H. Swan. Ann. Surg. 147:281-288 (March) 1958 [Philadelphia].

During the past decade many experiments were reported from which it was deduced that hypothermia has a beneficial effect on hemorrhagic shock. The authors, using different methods, were not able to corroborate this; on the contrary, there was evidence that hypothermia might impose a definite deleterious influence on the response of an animal to acute hemorrhage. In this study, 3 groups of adult splenectomized dogs were subjected to a hemorrhage of 35% of their measured blood volume. Group 1 included dogs bled in the normothermic state and served as a control. Group 2 comprised dogs that were cooled to 25 C (77 F) prior to hemorrhage. Group 3 consisted of dogs that were bled while normothermic and then cooled to 25 C (77 F). All the animals in groups 1 and 3 survived, while the animals in group 2 suffered an 80% mortality. Thus, hemorrhage in an already hypothermic dog is usually fatal, while hypothermia imposed on a dog just bled is not fatal with the bleeding volumes employed. The critical difference in the experience with these 2 groups of hypothermic animals was the existence in group 3 of a "grace period" (early cooling period) after hemorrhage, during which time compensations to the hemorrhage occurred. Hypothermia apparently altered the capacity of the dog to achieve circulatory compensation to acute hemorrhage. There was a close correlation between the blood pressure response to hemorrhage and survival. Only dogs that were bled after cooling (group 2) had a significant profound and prolonged hypotension. The value of hypothermia as a method of treatment for hemorrhagic shock is neither confirmed nor refuted by this study, but doubt is cast upon the rationale of its use. The hypothermic dog is unable to survive a hemorrhage volume which is nonfatal to the normothermic dog. Therefore, if operations are carried out under hypothermia, deficits in blood volume must be avoided.

BOOK REVIEWS

The Principles and Practice of Diathermy. By Bryan O. Scott, M.R.C.S., L.R.C.P., D.Phys.Med., Consultant in Physical Medicine, Radcliffe Infirmary, Oxford, England. Cloth. $5. Pp. 193, with 146 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1957.

Over half of this book is devoted to the basic physics and biophysics of short wave diathermy. These well-described, fundamental principles are as applicable in the United States as they are in the United Kingdom, and the use of British terminology should not trouble the American reader. The text gives scant attention to microwave diathermy, which apparently is far more widely used in the United States than in the United Kingdom. It is gratifying to note that the author clearly sets forth the medical reason for using diathermy, namely, its ability to heat tissues, and he does not contend that there are therapeutic nonthermal effects. There are good descriptions of the techniques of the medical application of short wave diathermy and appropriate recommendations as to safeguards and contraindications. There is an all-too-brief chapter on surgical diathermy. This text is recommended for use by any physician interested in diathermy. It should be of a special value in teaching the subject of short wave diathermy to medical students and physical therapy students.

Neuritis, Sensory Neuritis, Neuralgia: A Clinical Study with Review of the Literature. By Robert Wartenberg, M.D. Foreword by Wilfred Harris, M.D. Cloth. $8.50. Pp. 444, with 13 illustrations. Oxford University Press, 114 Fifth Ave., New York 11, 1958.

The late Robert Wartenberg has an established reputation as an outstanding clinician and teacher, an avid reader of the world literature of clinical neurology, a formidable critic, and a historian with tenacious devotion to the proper assignment of eponyms to signs and syndromes. These attributes are all evident in this monograph, published posthumously. The central thesis of the book is that there is a kind of neuritis which affects isolated and purely sensory nerves and which may attack different nerves over a period of many years. He describes nine cases of this type and labels the syndrome "migrant sensory neuritis." The remainder of the book is devoted to an analysis of the other major affections of peripheral nerves but relates to the central theme in an attempt to demonstrate that a general systemic disease can affect a single nerve and that either the motor or the sensory fibers in a mixed nerve may be injured. The pertinent literature is cited, and there are comments about the clinical features of such conditions as trigeminal neuralgia, sciatic neuritis, multiple cranial neuritis, and meralgia paresthetica.

The benefits to be derived from a review of the literature are illustrated in the author's critical analysis of the role of mechanical factors in sciatic syndromes and meralgia paresthetica. He clearly shows that sciatic pain is not always due to herniation of the nucleus pulposus, but this fact does not prove his statement that the involvement of the nerve is the result of a virus infection, nor is the latter thesis established by quotations from authorities, living or dead, who have expressed a similar opinion but have not presented any evidence to support their belief. Similar criticism may be directed to the author's advocacy of a viral cause for Bell's palsy, multiple sclerosis, and trigeminal neuralgia. The role of cold in the etiology of facial paralysis and sciatic pain, "abiotrophy" as a cause of atrophy of muscles innervated by the median nerve, involvement of peripheral nerves in acute poliomyelitis, a relationship between "migrant sensory neuritis" and multiple sclerosis, the dental origin of trigeminal neuralgia, and the concept of "latent neuritis" are some of the ideas advanced by the author which are not apt to meet general acceptance. Although highly speculative, the book is tersely written. It is interesting and will serve as a source of reference for syndromes of the peripheral and cranial nerves. It does not, however, provide a substitute for the description of these syndromes in the standard textbooks of neurology which are of most use to the practitioner.

Introduction to Enzymology. By Alan H. Mehler. Cloth. $10.80. Pp. 425, with illustrations. Academic Press, Inc. 111 Fifth Ave., New York 3, 1957.

The study of enzymes can properly be included as one facet in almost any book that deals with plant or animal life. It is, therefore, encountered in organic and physical chemistry, clinical medicine, plant physiology, bacteriology, biology, biochemistry, and many other sciences. Much of the investigative material in the rapidly expanding field of enzyme chemistry is somewhat isolated, and its full significance, therefore, is frequently not completely comprehended. This book is an outgrowth of a course in enzyme chemistry which the author taught to a group of investigators with varied interests. For this reason, it contains a different organization than is usually found in the many excellent monographs on enzymes that are available. The author has combined in various chapters those

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

enzymes which are involved in certain metabolic sequences, showing the interrelationships and mechanisms used and the multiplicity of factors involved in a particular sequence. Although the book is divided into nine chapters based on different metabolic sequences, enzyme chemistry is so interrelated that it is practically impossible to separate it effectively. The book contains a short introductory chapter that includes a brief history of enzyme chemistry and a short discussion of some general fundamental properties of enzymes. The metabolic sequences discussed in the following chapters include protein and peptide hydrolysis, fermentation and oxidation of metabolic fuels, the transfer of electrons, hydrogen and oxygen in biological oxidations, sugar and sugar derivatives, polynucleotides, amino acids, other acids and acid derivatives, and a final chapter on the part enzymes play in the organization of structure and function. Each chapter contains footnoted references to specific aspects of enzymes in addition to general references to the broad field under discussion at the end of the chapter. A subject index is also included.

Rand, Sweeny and Vincent's Growth and Development of the Young Child. By Marian E. Breckenridge, M.S., and Margaret Nesbitt Murphy, Ph.D. Sixth edition. Cloth. $5.50. Pp. 548, with 76 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftsbury Ave., London, W. C. 2, England, 1958.

Although this book is not strictly a medical textbook on child development, it does fill a gap in the literature by explaining some of the underlying causes of child growth and behavior. Essentially, what is presented is an attitude or philosophy that can be used in any study of children. For the paramedical cohort of the physician, this simple but scientific book provides insight into what makes the child "tick." The section on the child's physical equipment for growth, development, and functioning should be of aid to all who have to answer the worried parent's questions on a child's size and shape. The book's primary usefulness will be for students of child development, but it can also serve as a physician's reference textbook. It might be of value as a book to offer parents to confirm the physician's observations and conclusions. There is an excellent index. The style is unusually clear and concise for the material covered.

Methods in Surgical Pathology. By Henry A. Teloh, M.D., Assistant Professor of Pathology, Northwestern University Medical School, Chicago. Cloth. $4.75. Pp. 127, with 12 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1957.

This short manual describes the fundamental maneuvers which the author has found useful, as a pathologist, in examining specimens removed at operation. Particularly valuable are the emphasis on block selection and processing, the indication of inadequacy when simple diagnostic "tagging" rather than prognosis is the result of the examination, and the need for a 24-hour schedule between operation and report. Since this is a personal production, some pathologists may find minor points of difference with various portions of the book. All would not agree with the hesitancy about the use of frozen sections on endometrium, brain, thyroid, and lymph nodes, although the admission must be made that a definite diagnosis may have to be deferred until paraffin sections are examined on this group of tissues. Despite minor criticisms, the book is a pioneer effort which fills a serious need. In the hands of a first-year resident in pathology or a clinical resident on rotation through surgical pathology, it should prove valuable in shortening the period during which he feels lost when encountering surgical specimens for the first time. There is a place for such a manual in every laboratory of surgical pathology. With minor local revisions, according to individual laboratory practices, it should prove timesaving.

Drugs of Choice 1958-1959. Walter Modell, M.D., Associate Professor of Pharmacology, Cornell University Medical College, New York, editor. Cloth. $12.75. Pp. 931, with illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1958.

This book is a symposium of the opinions of 37 experts in therapeutics, including the editor, concerning the comparative effectiveness of drugs marketed in the United States. It is intended to serve as a practical guide to the selection of the best drug for a particular therapeutic problem, and it deals with a wide variety of purposes and situations for which drugs are generally used. Biological products have been purposely excluded, and no section on the selection of skin disinfectants was found. The subject matter comprises such topics as principles of the choice of drugs, the choice of drugs for children, the choice of a diuretic, and the choice of drugs for gastrointestinal disorders. Most of the chapters include discussions of the clinical applications and general pharmacological considerations, as well as of the classification and individual importance of the drugs involved. Selected references appear at the end of the chapters, together with a separately compiled drug index which describes various brands and dosage forms. The latter lists some drugs not mentioned in the text and some that are not generally available. A general index is also provided. Although the book is a commendable compendium of expert opinion concerning drugs of choice in today's materia medica, it is not the only source of unbiased information of this kind. Its large size makes it inconvenient for use as a practical guide. On the other hand, it should prove to be a worthwhile reference for students of medicine, clinicians, and members of allied professions who wish a comprehensive and critical treatise on the subject.

QUESTIONS AND ANSWERS

SUPPLY OF FLUIDS FOR PARENTERAL ADMINISTRATION

To the Editor:—*In a community hospital with 60 beds in medical, surgical, obstetric, and pediatric services and with a staff of 11 general practitioners and 1 surgeon, over the years the maintenance of a stock of intravenously given fluids has become confusing, due to the frequent additions of new mixtures by manufacturers. A committee is seeking information for ways of cutting down on the stock of these fluids and of still having available the required solutions for virtually all needs. Please give recommendations concerning the desirability of fructose and dextrose, whether both sugars should be included, and what electrolyte vials should be included in a full inventory.*

Michael A. McCall, M.D., Marion, N. C.

Answer.—It is not possible to give any simple rule-of-thumb answer to this inquiry. However, since fluids are frequently administered without due thought as to the reason for a particular choice, it may not be amiss to review some of the reasons for giving this form of therapy. These fluids should be given for specific purposes. The objectives of parenterally given therapy include the following considerations: (1) rehydration of cells and provision of fluid for urine formation and for insensible and other losses; (2) restoration of the volume of extracellular fluid; (3) restoration of the intravascular fluid volume; (4) supplying of calories to minimize catabolism; (5) correction of electrolyte disturbances associated with acidosis or alkalosis; and (6) prevention of deficiencies in specific electrolytes or other nutrients.

A particular parenterally given fluid is not equally effective for all purposes, although some fluids may be useful for several purposes. Usually more than one of the objectives listed above needs to be accomplished. For example, 0.45% of sodium chloride in a 5% dextrose solution can be used for rehydration of the cell, restoration of extracullular fluid, and provision of expendable fluid, as well as of some calories. However, more calories are frequently necessary than can be provided in a 5% dextrose solution without giving an excessive volume of fluid, particularly to a patient with anuria or oliguria. While acidosis and alkalosis can be combated to some extent by sodium chloride, its effectiveness depends on renal control of the relative amounts of sodium and chloride excreted, and this versatile substance does not provide for other ion deficiencies that may exist. For example, a potassium deficiency consistently accompanies an alkalosis and frequently occurs in a metabolic acidosis, particularly in the diabetic. The alkali reserve is more rapidly and effectively restored by sodium bicarbonate or lactate than by sodium chloride. The electrolyte depletion produced by chloride loss can only be adequately repaired by administration of both sodium and potassium chloride. Calories may be provided by a 10-20% dextrose solution or by invert sugar, but amino acid administration may be important if the patient is in a poor nutritional state or if prolonged dependence on parenterally given nutrition occurs. In addition, calcium administered by this method is sometimes essential, and magnesium and phosphate ions are also of importance in certain conditions. The use of invert sugar, which is half fructose and half dextrose, cannot be regarded as essential, although it may have some advantages in minimizing the tendency for hyperglycemia and glycosuria to occur from parenterally given sugar, particularly in patients with diabetes mellitus or liver diseases. It has been reported that fructose is less conducive to postinfusion hypoglycemia than dextrose, although it is not clear how frequent or important postinfusion symptoms may be in most subjects. There are several reliable commercial sources of parenterally given fluids, so that no preference need be expressed.

Answer.—It would be difficult to pick out the intravenously given fluids that would be specifically needed for a 60-bed hospital. Instead, a list of all such fluids that are used in a 300-bed general hospital follows. This hospital services all types of medical and surgical patients, and these fluids are adequate for its needs.

Alcohol (5%), in water, 1,000 cc.
Protein hydrolysate (5%), in dextrose solution, 1,000 cc.
Dextrose, *thiamine, riboflavin, nicotinamide, pyridoxine, vitamin* B_{12} *(5%), in saline solution,* 1,000 cc.
Dextrose (5%), in saline solution, 1,000 cc.
Dextrose (5%), in saline solution, 250 cc.
Dextrose (10%), in saline solution, 1,000 cc.
Dextrose (5%), in water, 1,000 cc.
Dextrose (5%), in water, 500 cc.
Dextrose (5%), in water, 250 cc.
Dextrose (10%), in water, 1,000 cc.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

Dextrose (10%), in water, 500 cc.
Dextrose (20%), in water, 500 cc.
Distilled water, 500 cc.
Invert sugar (10%), in water, 1,000 cc.
Invert sugar (10%), in saline solution, 1,000 cc.
Invert sugar (10%), potassium chloride (0.3%), in water
Invert sugar (10%), potassium chloride (0.3%), in saline solution
Invert sugar (10%), sodium, potassium, calcium, chlorine, lactate, magnesium, 1,000 cc.
Invert sugar (10%), sodium, potassium, chlorine, lactate, magnesium, phosphoric acid, 1,000 cc.
Invert sugar (10%), sodium, potassium, chlorine, ammonium, 1,000 cc.
Modified duodenal solution
Sodium chloride solution, isotonic, 1,000 cc.
Sodium chloride solution, isotonic, in 1,000-cc. pour-out bottles
Sodium chloride solution, isotonic, 250 cc.
Sodium chloride solution (5%), 1,000 cc.
Sodium chloride solution (0.45%), in water
Sodium lactate (1.87% molar solution)
Protein hydrolysate (5%), in water
Dextrose (5%), in sodium chloride solution (0.2%), 150 cc.
Dextrose (5%), w/v in sodium chloride solution (0.2%), 500 cc.
Dextrose (5%), w/v in sodium chloride solution (0.2%), 1,000 cc.

BLEEDING AND COAGULATION TESTS PRIOR TO TONSILLECTOMY

To the Editor:—*What is the latest opinion on the value and significance of preoperative coagulation and bleeding time determinations in patients requiring tonsillectomy? Is there any test that will forewarn one of a potential bleeding hazard that may exist even with a carefully done tonsillectomy and adenoidectomy?*

Robert S. Hamilton, M.D., Conrad, Mont.

To the Editor:—*The medical staff of a hospital is evaluating the necessity for routine performance of bleeding time and clotting tests preliminary to tonsillectomy and adenoidectomy. Please give information as to whether these tests are currently required as legal "common usage" or have been generally discontinued as being not significant.*

Robert C. Olson, M.D., Menominee, Mich.

Answer.—Most large clinical groups have abandoned routine determinations of coagulation and bleeding times among patients who are to undergo tonsillectomy. This has been done because so few instances of a bleeding abnormality were ever found without an accompanying history or physical finding of a hemorrhagic diathesis. The most important safeguard before tonsillectomy is performed is the obtaining of a satisfactory history from the patient or the patient's family. Any patient who has a history of easy bruising or a tendency toward bleeding should have a more thorough examination of his coagulation mechanism than simply determination of the coagulation and bleeding times. Determination of the bleeding time might detect pseudohemophilia or possibly unrecognized thrombocytopenic purpura, but it is rather unlikely that it would do so in the absence of an adequate history, which should serve as a warning. Determination of the coagulation time would not bring to light anything but hemophilia that happened to be active at the moment, and, even so, it is not uncommon to find patients with hemophilia in a relatively quiescent state who present a normal coagulation time. A definite history of bleeding in these patients would be most helpful, since mild hemophilia commonly creates much difficulty at the time of operation. Also, determination of the coagulation time might fail to detect a deficiency of prothrombin, as well as lack of some of the other coagulation factors. For these reasons it would seem best to direct questions toward antecedent bruising or bleeding, and, if such a history is obtained, a more thorough study of coagulation factors, as well as the platelet count, should be carried out. If no such history is obtained, it would be relatively safe to proceed with tonsillectomy.

Answer.—Routine coagulation and bleeding time determinations prior to tonsillectomy are valueless. Most of the determinations are done either in glass tubes or in glass capillaries. Frequently, the coagulation time, as determined by these methods, shows normal values even in cases of hemophilia. The best "test" is to question the patient carefully as to hemorrhagic disturbances, both in himself and in his family. The only tests that would actually forewarn one regarding a hemorrhagic disturbance would involve a complete hemorrhagic survey, which is unjustified for a minor operation. Under the circumstances, the best thing to do is to question the patient carefully and then have hemorrhagic tests done only in doubtful cases.

Answer.—For many years, many competent throat specialists have questioned the value of coagulation and bleeding time determinations as a routine measure. Instead, reliance has been placed primarily on a history of bleeding in the patient and the patient's family. A positive history should be followed by comprehensive physical and blood examinations, including coagulation and bleeding time determinations.

Answer.—At best, coagulation and bleeding time determinations performed preoperatively in persons requiring tonsillectomy and adenoidectomy are crude clinical procedures. In general, the slide method test for coagulability may be disregarded if findings show the time prolonged to no more than two or three times that accepted as normal. However, if results show an unusually prolonged time, the patient should have comprehensive physical and blood examinations.

SCREENING FOR DIABETES

To the Editor:—*Please comment on the following procedure to detect diabetes: First, a 24-hour urine specimen is examined for sugar and a blood sugar test is done one and one-half to two hours after a meal. If findings in the first test are positive and/or the blood sugar level is over 120 mg. %, a glucose tolerance test is done. If any one specimen in the glucose tolerance test has a level of over 160 mg. % and/or the blood sugar level does not return to the original value or normal after two hours, the patient is considered to have an abnormal or potentially diabetic curve. These are strict criteria, thus eliminating steroid provocation tests.*

M.D., Maine.

Answer.—Any screening procedure runs the risk of two opposite errors: (1) true cases of disease are missed, and (2) normal persons are falsely labeled as having the disease. Assuming that the method of determining blood sugar level referred to is that of Folin and Wu, which gives normal values of 80 to 120 mg. per 100 ml., the procedure outlined is sound in that it will rarely miss a case of true diabetes. Parenthetically, a postprandial blood sugar value much greater than 120 mg. per 100 ml.—say, 180 or higher—is diagnostic of diabetes, and a glucose tolerance test is not required. At the same time, the strict criteria that largely exclude false-negative results are apt to include some false-positive findings, that is, persons with such conditions as hyperthyroidism, gastrointestinal anastomoses, or starvation may be labeled diabetic when they are not. The inquirer recognizes this possibility when he refers to "abnormal or potentially diabetic" curves. The validity of borderline glucose tolerance curves for the diagnosis of diabetes must be determined by the exclusion of other conditions and, frequently, by further testing.

HEATING AND MULTIPLE SCLEROSIS

To the Editor:—*A 30-year-old woman has had multiple sclerosis for the past three years. Physiotherapy (such as hot baths) seems to help her most during troubled periods. She now plans to build a house and is concerned with what type of heating system to install. She appreciates that hot baths are good, but are there any real suggestions in favor of wall heat versus forced draft, steam, or solar heat?*

M. C. Florine, M.D., Janesville, Minn.

Answer.—The question brings up two considerations: 1. What, if anything, is there in heating that may influence the course of multiple sclerosis? 2. If there is a relationship, which type of heating would be most favorable? In answer to the first question, there is uniform agreement that chilling and infection, e. g., colds and sinusitis, are often events associated with a relapse. The second consideration, therefore, boils down to the choice of a system most likely to give heating throughout the house with minimum variation in temperature, minimal air movement or "drafts," and least drying effect on the mucous membranes because of low relative humidity. Though such considerations are largely empirical, most physicians would agree that these three environmental conditions do appear to play a role in the pathogenesis of acute upper respiratory infections. One may immediately eliminate solar heat as not pertinent to the discussion, since it refers to a choice of a source of energy for heating rather than to the type of heating system. Further, when this is used some kind of auxiliary conventional system is necessary. Steam heat is efficient, but, because the radiators present a large, exposed surface area at a high temperature, hot air currents are induced by convection. This effect is regarded as helping produce irregular temperature levels in the room and excessive drying of the mucous membranes. The same may be said for hot water heat, though to a lesser extent since the temperature of the radiators would be lower. Forced draft eliminates high temperature surfaces and drying, but the system must be carefully designed to avoid drafts. Radiant heat, attained by placing hot water pipes in floor, ceiling, or walls, is probably the best solution for uniform and healthful conditions. One may raise the point of living in a year-round warm climate. Although such an environment may appear to be desirable from the point of view of respiratory infections, it should never be considered if the move will raise economic and emotional problems.

POSITIVE FINDINGS IN HINTON SEROLOGIC TEST

To the Editor:—*A 26-year-old man, about to be married, showed positive findings in a Hinton serologic test. He was given a course of therapy with sterile procaine penicillin G with aluminum stearate suspension, 1 million units for 10 consecutive days. One month later, another Hinton test showed positive findings. How can the case be controlled and the patient cured? What is the latest treatment? Is a spinal fluid test advised? The patient did not contract any foreign diseases, and he does not remember any initial sore anywhere.*

S. B. Kaufman, M.D., Fall River, Mass.

Answer.—Apparently the serum of this patient was not titrated for units. It should be titrated despite the fact that he has had penicillin treatment; a low titer makes one suspicious of a false-positive serologic test. If a patient gives no history of having contracted syphilis and bears no physical or neurological signs to support such a diagnosis, one should always be suspicious of a false-positive serologic test. A Treponema immobilization (TPI) or some of its variants should be performed and re-checked. If findings in the TPI test are negative. then the patient does not have syphilis (98% accurate). If findings in the TPI test are positive. the patient does have syphilis. He should then have a complete physical and serologic examination, including examination of eyegrounds, roentgenogram of the chest to exclude cardiac and aortic changes. and spinal fluid examination to exclude central nervous system syphilis. In the event that findings in the TPI test are positive and those in all of the other tests, including the spinal fluid examination. are negative, then the patient should have at least two more courses of therapy with penicillin, 10 million to 12 million units given in doses of 1 million units each and repeated again after three months (long-acting penicillin given twice a week). The serum should be titrated three months after each course of treatment. If findings in the TPI test are negative, it means that this man may be, at the present time, suffering from one of the hidden collagen diseases. At least 25% of such persons have been known to develop such diseases. Also, it is possible that he may have contracted malaria or some other infectious disease which could be responsible for the false-positive serologic test.

SERUM CHOLINESTERASE AND MYASTHENIA GRAVIS

To the Editor:—*A patient who has proved myasthenia gravis at present is taking neostigmine and doing fairly well; however, in the course of his illness he suffered a cerebral thrombosis, and a laboratory examination was done. Because he had worked in greenhouses all his life and had been in contact with numerous and varied insecticides, a serum cholinesterase determination was made. The level was abnormally low and has been repeatedly so. Is there any information available regarding cholinesterase levels in patients with myasthenia gravis?*

John M. Gunsolus, M.D., Stuart, Fla.

Answer.—Serum cholinesterase determinations have been reported in patients with myasthenia gravis since 1939. The first reports in the literature stated that levels of untreated patients were higher than normal and that such drugs as neostigmine, when injected, would reduce them to normal or below normal ranges. A number of more carefully worked out determinations, in which the level of cholinesterase in the red blood cells was determined as well as that in the serum. showed that the resting levels of patients with myasthenia gravis who were not under treatment were within normal ranges. It has been agreed essentially that injection of an anticholinesterase, such as neostigmine. will reduce the serum cholinesterase level slightly, and. in overdosage of this medicine, in either normal persons or patients with myasthenia, lower levels will be encountered. Such substances as the alkyl phosphates, when taken in excess. will result in very low serum cholinesterase levels, and this will persist for some weeks or months. In the case reported, since the patient is taking neostigmine, one would expect that the cholinesterase level might be normal or slightly low. This consultant has no evidence that chronic residuals from insecticides affect the level of serum cholinesterase.

AMENORRHEA AND ABDOMINAL MASS

To the Editor:—*A 15-year-old girl has amenorrhea of four months' duration but no other symptoms of consequence. Her catamenia started at 12 years of age and was regular every 29 days until four months ago. Physical examination is essentially normal, except for slight obesity and, on rectal examination only (because of the intact hymen). a cystic mass which was felt in the right adnexa. It was about 7 by 7 by 6 cm., freely movable, and painless. The patient was reexamined two weeks later, and the same mass was palpated. A roentgenogram of the abdomen and an intravenous pyelogram were done, and findings were reported by the radiologist as negative. Should dilation and curettage be done while the patient is being examined under anesthesia prior to laparotomy for the cyst?* *M.D., Florida.*

Answer.—Before examination under anesthesia is done. pregnancy tests are suggested. A uterine probe would help to determine whether the mass is uterine or adnexal. If it is adnexal. laparotomy should be done, and if it is uterine, waiting another month for observation would enhance the chance of making an accurate diagnosis both by x-ray and bimanual examination. If the diagnosis is still uncertain, then dilation and curettage would be indicated and future treatment predicated on the findings.

MONOZYGOTIC OR DIZYGOTIC TWINS

To the Editor:—*A woman whose blood group is O, Rh negative, and subtype cde/c has male twins with blood group O, Rh positive, and subtype CDe/c. The mother has congenital coloboma of the irises, and one of the twins has this same anomaly. The pathologist's report on the placenta is twin fused placenta with double sacs which have a double wall. There are two cords. Is it possible on the basis of this information to state definitely that these are single or double ovum twins?*

Robert R. Livingston, M.D.
Glenwood Springs, Colo.

Answer.—The Rh information in this question is not helpful in determining whether the twins in question are from a single ovum or a double ovum. Nesbitt (Perinatal Loss in Modern Obstetrics. London, H. K. Lewis & Co., 1957) has recently stated. "The ability to determine the origin of twins from the relations between the placenta and its membranes has been questioned in recent years.... The placenta and membrane relations will, in most instances, however, show whether the twins are from one or two eggs. The one fallacy in this method is that at least 20% of monozygotic twins are not monochorial but are dichorial, and therefore at least 10% of all dichorial placentae do not belong to dizygotic but to monozygotic pairs.... Contrariwise, however, all monochorial placentae belong to monozygotic pairs." One could conclude, therefore, that the twins referred to in this question are not identical twins from two ova, although there is about a 10% chance that they are identical twins from the same ovum.

PAINTING DURING PREGNANCY

To the Editor:—*There is a prevalent belief that pregnant women should not paint or in any way expose themselves to paint fumes, because the turpentine in paint fumes might cause abortion. Is there any basis in fact for such precautions? If so, would the use of paints containing no turpentine be permissible?*

Melvin A. Marousek, M.D., Belle Fourche, S. D.

Answer.—There is no basis for the belief that the paint which is available today and used either for art or for ordinary decorative purposes, such as painting furniture or closets, will cause an abortion.

CARPE BOSSU DISEASE

To the Editor:—*What is the condition known as Carpe Bossu disease?* *M.D., Connecticut.*

Answer.—The condition called Carpe Bossu disease is one in which there is a ninth carpal bone, referred to as the carpal styloid bone, at the base of the third metacarpal. It may become quite painful and be associated with tenderness and swelling. The condition should be coded as 233-031.x Supernumary carpal bone with disturbance of function.

ALLERGY TO MUSHROOMS

To the Editor:—*Regarding hypersensitivity to mushrooms, a question on which appeared in the Questions and Answers section of* The Journal, *March 8, 1958, page 1262, it is important to point out that it is a common fallacy today that gastrointestinal disturbances to a food imply allergy to the inciting substance. Although the relationship of symptoms to ingestion of mushrooms in the case cited would seem to be unquestionable, it would be valuable to know whether the patient really had an allergy. The reaction might well be one of nonimmunological intolerance. There are many nonspecific irritant or toxic principles in mushrooms in small concentration, to which reactions comparable to that of favism to the pollen or beans of Vicia fava may occur. These affect only a few individuals predisposed to react to these small amounts. Further, the drying or dehydrating which renders a food nonallergenic (Fries and Glazer,* J. Allergy **21:** *169, 1950) usually destroys naturally contained irritants as well. Positive findings in skin tests for gastrointestinal disorders are rarely obtained, although in this instance of such severe symptomatology they might be seen. For reasons of safety, scratch tests should be done first, and only later the more sensitive intracutaneous tests should be made. As the consultant has implied, desensitization through the parenteral route is hazardous and through the oral route ineffective. The patient should learn to avoid gravies and dressings.*

Joseph Harman Fries, M.D.
Lakeville Medical Center
2035 Lakeville Rd.
New Hyde Park, N. Y.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*The statement that heating and drying of a food distinctly lessens its antigenicity is quite right. Fresh bananas and extracts of fresh bananas can constitute potent allergens and can cause anaphylactic shock, as well as urticaria and gastrointestinal symptoms. Other foods, too, e. g., milk and eggs, are also less allergenic when they are heated and/or dried. Nevertheless, mushooms are a form of yeast and can be potent allergens, and, in the patient under consideration, fresh mushrooms always led to severe reactions—dried mushrooms did not. If this phenomenon is an allergic one, and this consultant is convinced it is, the patient should be allergic and should show this by a positive scratch test for mushroom extract; if the scratch test is negative, an intradermal test should be done (1:1,000). In addition, the patient should exhibit other evidences of allergy, e. g., family inheritance, blood eosinophilia, or other allergies. If findings in all these tests prove negative, then and only then would this consultant believe that the symptoms could have a nonallergic basis. Mushrooms are readily eaten by almost all people; they are not in the same class as peppers and other spices. Coca and associates (Hypersensitiveness, Anaphylaxis, Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1931, p. 438) make this comment: "Mushrooms are used fresh, canned, dried, and powdered. They are useful for flavoring soup, beef tea, and a number of other foods. The juice pressed from mushrooms, seasoned with spices, is employed in the preparation of catsup to be used as such or as a base for other sauces."*

WASHINGTON NEWS

FROM THE WASHINGTON OFFICE OF THE AMERICAN MEDICAL ASSOCIATION

Social Security Hearings Open . .
Labor Conference Opposes Free Choice . .
Medical Spending Due to Rise . .

COMMITTEE DECIDING ON FORAND BILL AND OTHER SOCIAL SECURITY ISSUES

After two full weeks of day-long hearings, the House Ways and Means Committee now is scheduled to decide behind closed doors what action to recommend on the Forand bill and other proposals for liberalizing social security.

Witnesses representing a cross-section of the country's commercial, professional, labor, and business life paraded before the committee, which now must sort out from the scores of proposed amendments those it expects to get through Congress in the limited time before adjournment, tentatively set for mid-August.

Proposals were as varied as the witnesses. Some of the witnesses advised the committee to hold fast with the benefits at their present rates, pending further study. Others wanted moderate changes, with minor tax increases or no change in tax rates or base. Still others wanted benefits and taxes boosted as much as 100%.

Heading off the parade of witnesses, Secretary Folsom of the Department of Health, Education, and Welfare guardedly indicated that the administration probably would find a slight increase in benefits acceptable. An 8% boost was suggested for those who retired before 1954 (when on the average their earnings would entitle them to less) and a 3% increase for those who have since retired.

Mr. Folsom said this could be financed safely by increasing the amount of wages on which old-age and survivors insurance taxes are levied from the present $4,200 to $4,800 but without boosting the tax, now at 2¼% for employer and employee each and 3⅜% for the self-employed.

However, the secretary said he was opposed to further U. S. contributions to public assistance and that he thought the matching formula now in use should be changed so states with relatively low per capita incomes would receive relatively more U. S. help.

Mr. Folsom also said his department planned to propose bringing the medical care section of public assistance grants within the ceiling. He explained that HEW wanted more time to evaluate problems of the disability payments program before deciding whether the definition of disability should be changed. There is pressure to have it modified.

The Forand bill—for payment of medical care and hospital-nursing home costs of social security beneficiaries—was not touched on by the secretary in his prepared statement. However, Rep. Aime J. Forand (D., R. I.) questioned him about this. Mr. Folsom said he would not favor the idea, nor an "optional" Forand plan, which he said wouldn't work.

The secretary then went on to describe the "tremendous increase in the volume of hospitalization insurance." He cited a 1957 survey by HEW which showed that at least 43% of those over 65 were covered, and he discussed a new concept, increasing in popularity, for the employer to buy post-retirement insurance for his employees.

Urging the committee to hold up action of the Forand type at least until an investigation of social security is completed by next January, he said insurance expansion and increasing attention to nursing homes and chronic disease facilities were helping to solve the problems of medical care financing for the aged.

Among other witnesses testifying in opposition to the Forand bill was Ira O. Wallace, president of the American Nursing Home Association. He said that while his association favored a more liberal policy by the Federal and other governments toward indigents, "We feel that any proposal for the government to enter into contractual agreement to reimburse medical facilities, physicians, and dentists for their services, places the federal government in a paternalistic role. . . . The government could deny the recipient free choice of facility and service."

Favoring the Forand principle was Sen. William Proxmire (D., Wis.), who testified on behalf of his own bill which would greatly liberalize all phases of social security as well as set up a hospital-surgical program for beneficiaries.

"The cruelest costs of old age are medical costs," he said. "Illness that exacts heavy doctor bills and hospital bills is the handmaiden of old age."

Senator Proxmire declared that insurance premiums are too high for older people in the few cases where they can get into a program.

To finance his total program, the senator would lift the OASI payroll tax from the present 2¼% on employer and employee to 3½% and from 3⅜% to 5¼% on the self-employed. The present law taxes income up to $4,200; the Proxmire plan would push the cutoff to $7,500.

In a lively exchange, Rep. John W. Byrne (R., Wis.) reminded the senator that his plan would mean an additional tax of $168 (177.8% increase) for those earning $7,500 in salary and a $252 increase for the self-employed. "The burden would be on the low-income families," Mr. Byrne declared.

Three welfare representatives also testified for the Forand bill. They were George McLain, representing the National Institute of Social Work; Patrick A. Tompkins, Massachusetts commissioner of public welfare; and Ellen Winston, president of the American Welfare Association and welfare comissioner for North Carolina.

Rep. John W. McCormack (D., Mass.), majority leader in the House, testified in favor of his bill that would permit use of the vendor system of payments for all U. S. medical grants under the ceiling for each category in public assistance.

(Continued on next page)

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Lown, B., and Levine, S. A.:
Current Concepts in Digitalis Therapy, Boston,
Little, Brown & Company, 1954, p. 23, par. 2.

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LABOR HEALTH OFFICERS' CONFERENCE OPPOSES FREE CHOICE OF PHYSICIAN

A national conference of doctors administering union health plans and others interested in third-party medicine met for two days in Washington to discuss their problems. With few exceptions, participants agreed that patients could receive better care without free choice of physician and hospital.

During the course of the meeting, sponsored mainly by the United Mine Workers Welfare and Retirement Fund, the American Medical Association restated its position that free choice of physician is a basic guarantee of good medical care and that miners "have been subordinated to the financial interests of the UMW fund."

Dr. Warren F. Draper, executive medical director of the UMW fund, told the group that the fund would never return to free choice of physicians. "In order to continue to provide its present liberal medical and hospital benefits, the trust fund will deal only with those physicians and hospitals which it considers necessary and essential," Dr. Draper declared.

He then took in other union health plans with these words: "It is the right of all labor health services to control their own medical care programs, and they must insist on this right if the cost of medical care for their people is to be kept within reasonable bounds." Dr. Draper said the great majority of doctors serving mine workers fully understand the position and problems of the fund and are doing "their utmost to cooperate with the fund in providing a high quality of medical service."

In a statement issued on the second day, Dr. F. J. L. Blasingame, general manager of the A. M. A., stated that the controversy "actually arises from the conflicting viewpoints of organized medicine and the third party in the doctor-patient relationship, and the right of the third party to judge the competence of physicians." He said the A. M. A. has tried repeatedly over a long period of time to establish the kind of harmonious relationships between physicians and third parties which could result in the provision of the highest quality of medical care for the individual patient.

"As things stand today, there is no question but what the medical interests of the miner and his family have been subordinated to the financial interests of the fund," Dr. Blasingame stated. "By controlling millions of dollars put into the trust fund by industry . . . Dr. Warren Draper on behalf of a small group of trustees has been able to establish a controlled and highly paternalistic medical care program and their families in which their personal choice of physician has been abrogated."

Horace Hansen, general counsel of Group Health Federation of America, advised the delegates to keep close track on acts of local medical societies in connection with doctors who participate in third-party health plans and to be prepared to seek recourse in the courts. He said lay groups of all kinds have a legal right to "buy medical care for their members" and beneficiaries and that doctors have a legal right to render them medical care by any method of compensation which is mutually agreeable. He maintained that medical societies that take disciplinary action against doctors or induce hospitals to refuse service are in restraint of trade.

Dr. Ray E. Trussell of Columbia University's School of Public and Administrative Medicine reminded the conferees that most of the problems aired at the conference really center around "a small group of doctors who do not agree with you and with whom you don't agree." He said he has found that organized medicine can be "friendly and constructive" in working out the provision of medical care.

SPENDING BY HEW FOR NEXT YEAR GOING UP

Sharp increases in medical spending by the Department of Health, Education, and Welfare—amounting to $231,514,000 more than the House allowed—have been proposed by the Senate Appropriations Committee. The total HEW budget for the fiscal year just beginning would be nearly 10% higher over-all than the House voted earlier in the session—$2,796,594,581 as compared to $2,565,080,581.

The Hill-Burton hospital construction program would be increased by about 70%, with the Senate committee voting the full authorized amount—$211,200,000 for building an estimated 31,800 beds in hospitals, nursing homes, and chronic disease units as well as for construction of diagnostic and treatment centers and rehabilitation facilities. The House had settled on $121,200,000.

Medical research spending would rise at a rate of more than 45% under the Senate proposals. Expressed in dollars, the increase is about 101 million dollars, with all seven institutes profiting from the committee's generosity.

Here are specific figures in the research field: National Cancer Institute, an increase of $23,706,000; for a total of $81,129,000; Mental Health Institute, up $15,499,000 for a total of $55,896,000; National Heart Institute, $13,317,000 to $49,529,000; Arthritis and Metabolic Disease Institute, $13,306,000 to $34,798,000; Allergy and Infectious Disease Institute, $8,503,000 to $26,500,000; Institute of Neurological Diseases and Blindness, $10,273,000 to $32,250,000; and Dental Health Institute, $1,380,000 to $6,543,000.

The committee decided to appropriate new funds for projects not even considered by the House. One of these is the National Library of Medicine, which would get $6,950,000 for its long-delayed new home on the grounds of the National Institutes of Health at Bethesda. The committee also recommended a $9,625,000 item for a general office building at Bethesda for the NIH and it burgeoning activities.

Un-earmarked funds for medical research known as general research and services were nearly doubled, from $17,742,000 to $32,552,000. And for medical schools and others doing research, the committee complied to a request that the 15% ceiling on allowance for overhead costs in research projects be eliminated.

For stepped-up training for public health workers, the committee proposed 5 million dollars, an increase of $2,800,000 over the House proposal. For graduate nurse training grants, the group proposed an increase of 4 million dollars; current spending is 3 million dollars. For Indian health activities, the Public Health Service would get another $4,775,000 for a total of 45 million.

Commenting on its action in the research field, the committee stated: "The committee has heard incontrovertible testimony on urgent unsolved medical research problems, cited specifically in the committee's reports on the individual institutes. Such testimony shows that scientists and adequate facilities are available to begin the attack on these problems now."

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1958 Clinical Meeting, Minneapolis, Dec. 2-5.
1959 Annual Meeting, Atlantic City, June 8-12.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.

AMERICAN

June

American Proctologic Society, Los Angeles Statler, Los Angeles, June 29-July 3. Mr. Norman D. Nigro, 10 Peterboro St., Detroit 1, Executive Secretary.

July

American College of Surgeons, Sectional Meeting, Concert Hall, Stockholm, Sweden, July 2-7. Dr. Michael L. Mason, 40 E. Erie St., Chicago 11, Chairman.

American Society of Facial Plastic Surgery, New York, July 16. Dr. Samuel M. Bloom, 123 E. 83d St., New York 28, Secretary.

Idaho State Medical Association, Sun Valley, July 6-9. Mr. Armand L. Bird, 364 Sonna Bldg., Boise, Executive Secretary.

Intermountain Pediatric Society, Sun Valley, Ida., July 4-6. Dr. Thales H. Smith, 220 N. University Ave., Provo, Utah, Secretary.

Rocky Mountain Cancer Conference, Shirley-Savoy Hotel, Denver, July 9-10. Alexis E. Lubchenco, 835 Republic Bldg., Denver 2, Chairman.

United States Section, International College of Surgeons, Eastern Regional Meeting, Manchester, Vt., July 1-5. Dr. M. Leopold Brodny, 636 Beacon St., Boston, General Chairman.

August

American Congress of Physical Medicine and Rehabilitation, Philadelphia, Bellevue-Stratford Hotel, Aug. 24-29. Dr. Frances Baker, 1 Tilton Ave., San Mateo, Calif., Secretary.

American Hospital Association, Palmer House, Chicago, Aug. 18-21. Dr. Edwin L. Crosby, 18 E. Division St., Chicago 10, Director.

American Veterinary Medical Association, Sheraton Hotel, Philadelphia, Aug. 18-21. Dr. J. G. Hardenbergh, 600 S. Michigan Blvd., Chicago 5, Executive Secretary.

Biological Photographic Association, Shoreham Hotel, Washington, D. C., Aug. 19-22. Miss Jane Waters, Box 1668, Grand Central P. O., New York 17, Secretary.

Chemical Organization of Cells, Normal and Abnormal, Madison, Wis., Aug. 21-23. Dr. J. F. A. McManus, Univ. of Alabama Medical Center, Birmingham, Ala., Chairman.

International College of Surgeons, Regional Meeting, Western Section, The Riverside Hotel, Reno, Nev., Aug. 21-23. For information address: Dr. Leo D. Nannini, 190 Mill St., Reno, Nev.

National Medical Association, Hotel Schroeder, Milwaukee, Aug. 11-14. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Northwest Proctologic Society, Sun Valley, Ida., Aug. 27-29. Dr. John McKay, 645 Medical Dental Bldg., Seattle, Secretary.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 15-17. Dr. John H. Freed, Denver 20, Secretary.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 21-23. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

World Medical Association, Copenhagen, Denmark, Aug. 15-20. Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, Secretary-General.

September

American Academy for Cerebral Palsy, Sheraton-Biltmore Hotel, Providence, R. I., Sept. 25-27. Dr. Raymond R. Rembolt, University Hospitals, Iowa City, Ia., Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 4-6. Dr. E. Stewart Taylor, 4200 E. 9th Ave., Denver 20, Secretary.

American College of Physicians, Mid-West Regional Meeting, Milwaukee, Wis., Sept. 27. Dr. James F. Gleason, 7 S. Oxford Ave., Atlantic City, N. J., General Chairman.

American Fracture Association, Skirvin Hotel, Oklahoma City, Okla., Sept. 29-Oct. 4. Dr. H. W. Wellmerling, 610 Griesheim Bldg., Bloomington, Ill., Secretary.

American Medical Writers' Association, Hotel Morrison, Chicago, Sept. 26-27. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Roentgen Ray Society, Shoreham Hotel, Washington, D. C., Sept. 27-Oct.3. Dr. C. Allen Good, 200, 1st St. S. W., Rochester, Minn., Secretary.

Colorado State Medical Society, Broadmoor Hotel, Colorado Springs, Sept. 24-27. Mr. Harvey T. Sethman, 1612 Tremont Place, Denver 2, Executive Secretary.

Kansas City Southwest Clinical Society, Municipal Auditorium, Kansas City, Mo., Sept. 22-25. Mr. A. L. Bingham, 3036 Gillham Rd., Kansas City 8, Mo., Executive Secretary.

Kentucky State Medical Association, Brown Hotel, Louisville, Sept. 23-25. Mr. J. P. Sanford, 1169 Eastern Parkway, Louisville 17, Executive Secretary.

Michigan State Medical Society, Sheraton-Cadillac Hotel, Detroit, Sept. 30-Oct. 3. Dr. L. Fernald Foster, 606 Townsend St., P. O. Box 539, Lansing, Mich., Secretary.

Mississippi Valley Medical Society, Morrison Hotel, Chicago, Sept. 24-26. Dr. Harold Swanberg, 510 Main St., Quincy, Ill., Secretary.

Montana Medical Association, Northern Hotel, Billings, Sept. 11-13. Mr. L. R. Hegland, P. O. Box 1692, Billings. Executive Secretary.

Nevada State Medical Association, Elko, Sept. 17-20. Mr. Nelson B. Neff, P. O. Box 188, Reno, Executive Secretary.

New Hampshire Medical Society, Mt. Washington Hotel, Bretton Woods, Sept. 19-22. Mr. Hamilton S. Putnam, 18 School St., Concord, Executive Secretary.

Northeastern Section, American Urological Association, Equinox House, Manchester, Vt., Sept. 12-13. Dr. F. O. Harbach, 831 James St., Syracuse, N. Y., Secretary.

Oregon State Medical Society, Columbia Athletic Club, Portland, Sept. 3-5. Dr. Max H. Parrott, 1020 S. W. Taylor St., Portland 5, Secretary.

Texas Academy of General Practice, San Antonio, Tex., Sept. 22-24. Mr. Donald C. Jackson, 1905 N. Lamar, Austin, Tex., Executive Secretary.

Tri-State Medical Society, Shreveport, La., Sept. 18. Dr. J. C. Sanders, Sanders Clinic, Kings Highway, Shreveport, La., Secretary.

United States Section, International College of Surgeons, Atlantic City, N. J., Sept. 7-11. Dr. Karl Meyer, 1835 W. Harrison, Chicago, Secretary.

Utah State Medical Association, Hotel Utah, Salt Lake City, Sept. 9-12. Mr. Harold Bowman, 42 S. Fifth East St., Salt Lake City 2, Executive Secretary.

Vermont State Medical Society, Mt. Washington Hotel, Bretton Woods, N. H., Sept. 20-22. Mr. Getty Page, 128 Merchants Row, Rutland, Vt., Executive Secretary.

Washington State Medical Association, Davenport Hotel, Spokane, Sept. 14-17. Mr. Ralph W. Neill, 1309 7th Ave., Seattle, Executive Secretary.

October

American Academy of Ophthalmology and Otolaryngology, Palmer House, Chicago, Oct. 12-17. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Secretary.

American Academy of Pediatrics, Palmer House, Chicago, Oct. 20-23. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill., Executive Secretary.

American Association of Medical Clinics, Palace Hotel, San Francisco, Oct. 2-4. Dr. John R. Hand, 1216 Southwest Yamhill St., Portland, Ore., Secretary.

American Association of Medical Record Librarians, Statler Hotel, Boston, Oct. 13-16. Miss Doris Gleason, 510 N. Dearborn St., Chicago 10, Executive Director.

American Association of Public Health Physicians, St. Louis, Oct. 27-31. Dr. Joseph M. Bistowish, P. O. Box 1117, Tallahassee, Fla., Secretary.

American Association for the Surgery of Trauma, Drake Hotel, Chicago, Oct. 2-4. Dr. William T. Fitts, Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American Clinical and Climatological Association, Otesaga Hotel, Cooperstown, N. Y., Oct. 9-11. Dr. Marshall N. Fulton, 124 Waterman St., Providence 6, R. I., Secretary.

American College of Gastroenterology, Jung Hotel, New Orleans, Oct. 19-25. Mr. Daniel Weiss, 33 W. 60th St., New York 23, Executive Secretary

American College of Surgeons, Oct. 6-10. Dr. Michael L. Mason, 40 E. Erie St., Chicago, Secretary.

American Dietetic Association, Bellevue-Stratford Hotel, Philadelphia, Oct. 21-24. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Heart Association, Fairmont Hotel, San Francisco, Oct. 24-28. Mr. John D. Brundage, 44 E. 23d St., New York 10, Secretary.

American Otorhinologic Society for Plastic Surgery, Conrad Hilton Hotel, Chicago, Oct. 12. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Public Health Association, Kiel Auditorium, St. Louis, Oct. 27-31. Dr. Berwyn F. Mattison, 1790 Broadway, New York 19, Secretary.

American School Health Association, St. Louis, Oct. 26-31. Dr. A. O. DeWeese, 515 E. Main St., Kent, Ohio, Secretary.

American Society of Anesthesiologists, Penn-Sheraton Hotel, Pittsburgh, Oct. 19-24. Dr. J. Earl Remlinger, 802 Ashland Ave., Wilmette, Ill., Secretary.

American Society of Plastic and Reconstructive Surgery, Drake Hotel, Chicago, Oct. 12-17. Dr. Kenneth L. Pickrell, Duke Univ. Hosp., Durham, N. C., Secretary.

Association of American Medical Colleges, Ocean House, Swampscott, Mass., Oct. 13-15. Dr. Dean F. Smiley, 2530 Ridge Ave., Evanston, Ill., Secretary.

Association of Life Insurance Medical Directors of America, Statler Hotel, Hartford, Conn., Oct. 22-24. Dr. Royal S. Schaaf, P. O. Box 594, Newark 1, N. J., Secretary.

Association of Medical Illustrators, Dallas, Tex., Oct., Miss Rose M. Reynolds, 42d & Dewey Ave., Omaha 5, Secretary.

Association of State & Territorial Health Officer: Hotel Washington, Washington, D. C., Oct. 22-24. Dr. Mack I. Stanholtz, State Office Bldg., Richmond, Va., Secretary.

Central Association of Obstetricians and Gynecologists, Hotel Leamington, Minneapolis, Oct. 2-4. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

Central Neuropsychiatric Association, Deshler Hilton Hotel, Columbus, O., Oct., 17-18. Dr. Ralph M. Patterson, Ohio State Univ., College of Med., Columbus 10, O., Secretary.

Central Society for Clinical Research, Drake Hotel, Chicago, Oct. 31-Nov. 1. Dr. Austin S. Weisberger, 2065 Adelbert Rd., Celeveland 6, Secretary.

Clinical Orthopaedic Society, Brown Palace Hotel, Denver, Oct. 2-4. Dr. Charles H. Franz, 1801 Wealthy St. S. E., Grand Rapids, Mich., Secretary.

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PHYSICIANS TO THE WORLD

PRESIDENT'S ADDRESS

Gunnar Gundersen, M.D., La Crosse, Wis.

IN ACCEPTING the office of President of the *American Medical Association*, I do so with deep feelings of appreciation, humility, and responsibility. My sense of responsibility is heightened by realization of the tremendous number and variety of challenges which medicine faces today. As individual physicians, members of organized medicine and citizens in the community and the nation, we have in recent decades encountered an ever-increasing complexity of demands on our time and thought. Now, like all of our fellow Americans, we find our problems compounded by the world struggle for survival and freedom—in the new age of hydrogen bombs, ballistic missiles, and earth satellites.

In recent years the individual physician has had an increasingly difficult time in trying to keep up with the accelerated scientific advances in medicine. Now, with man probing into outer space, it appears that our scientific future will be further complicated by the development of still another specialty—space medicine. Nevertheless, right here on terra firma it is more than ever true that medicine is a lifelong study—one which actually is just beginning when the young doctor receives his M.D. degree or completes his graduate training.

Meanwhile, we also are reemphasizing the emotional, personal, and spiritual factors in medical care. The age-old art of medicine—that intangible element made up of compassion and warmth—is regaining its proper place. In medicine, as in all other phases of American life, we are rediscovering that philosophy is just as important as technology, that the human personality cannot be subordinated to crisp efficiency.

The challenge of how to apply the science and art of medicine is formidable enough in itself. But it too has been further complicated by the changing backdrop on the American scene. Over the past 20 years we also have been called upon to consider a snowballing trend of social, economic, and political developments affecting medicine.

These problems are related to still another area—one in which we have obligations and responsibilities shared by all our fellow Americans. This is the broad arena of citizenship. We as individuals have the duty to bring our weight to bear on the vital question of whether the individual or the state shall stand supreme in America's future.

Obligations of the Physician

Certainly, one might say, all of that should be more than enough to ask of a physician or his profession—scientific excellence, concern for the patient as a human being, active effort to solve medicine's socioeconomic problems, and full discharge of the responsibilities of citizenship. I would, however, call your attention to still another challenge, still

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Read before the 107th Annual Meeting of the American Medical Association, San Francisco, June 24, 1958.

another set of demands. In this day and age—a time of terrible decision—we also must consider our obligations to all of humanity. As both physicians and citizens we must see that medicine plays its full role, not only in promoting better world health but also in helping the search for brotherhood and peace.

Some of you may be saying to yourselves, "With all our local, state, and national problems, how can we possibly find time to do anything about world health? What is the connection?" That, of course, is a natural reaction in view of the growing complexity of our professional life.

I would answer in two ways—one dealing with tradition and one with the realities of the present. The traditions of modern medicine began many centuries ago with Hippocrates, the Greek physician and teacher. Students from all over the Aegean area gathered around him on the island of Cos. From there they returned home to spread the knowledge and ethics which Hippocrates had taught them. And it is important to remember that when Hippocrates wrote the medical oath which all of us have taken he was speaking not just to and for Greeks; his words speak a universal language that applies to all men. So, ever since those distant days on the island of Cos, dedicated physicians have made their knowledge and compassion available to all who needed them.

Turning to present-day realities, I am convinced by personal experience that our medical heritage—which stems from Hippocrates—can be applied more widely, more effectively, in today's troubled world. As many of you know, I have been active for several years in the affairs of the World Medical Association. As a delegate in its General Assembly and a member of its Council, I have had the opportunity to meet hundreds of physicians from more than 50 countries. And I have learned that they sincerely desire closer understanding and cooperation—not only on scientific and professional matters but also on a human basis. There is growing recognition that medicine, with its resources and influence fully mobilized, can perhaps do more for world peace than the billions of dollars being poured into armaments. There is mounting conviction that the time has come when medical statesmanship must be used to augment the methods of political diplomacy.

I firmly believe that we can and must expand our vision and face up to this new challenge. The problems which trouble us here at home exist also for the physicians and peoples of other lands. The knowledge, ideas, and experience which we have gained can help them. But we also can benefit from learning more about their difficulties—how they might have avoided some, how they are trying to solve others. Our international obligations are simply extensions of our local responsibilities.

The common thread is a concern for human life and health, a respect for personal freedom and dignity. In my opinion, there is a clear, logical, mutuality of interest.

If we think we have difficulty in keeping up with medical advances, let us consider the thousands of physicians, nurses, and technicians throughout the world who carry on their work with only a fraction of the facilities, equipment, journals, books, exhibits, and other aids which are available to us. For many of them, just this one-week meeting in San Francisco would be the professional event of a lifetime.

If we think that our patients should have more sympathy and understanding, we who are bestowed with the blessings of our country must consider the millions of persons in other parts of the world who are diseased, undernourished, crippled, or dying. To them, just one kind look, one gentle word, one soothing drug would be like a miracle.

If we think that we have socioeconomic problems in American medicine, let us consider the plight of physicians and patients in those countries where there are extreme shortages of doctors, where people still pay medicine men and witch doctors for their incantations, or where medical care long has been used as a political football. In the latter case, let us learn well the lesson of medical unity.

If we think that our freedoms are threatened here at home, let us consider the millions who already have been subjugated by authoritarian philosophies or who are being victimized by constant, ruthless pressure and exploitation in the cold war between communism and democracy—a war that really can be won only by ideas, not by missiles or bombs.

As physicians, our first obligation is, of course, to our patients. But as members of the medical profession, our obligation extends to all mankind.

The Physician and World Peace

As American citizens our first duty is to this country. But as members of a civilization which believes in the brotherhood of man, we also have a duty toward all men who yearn for freedom, dignity, peace, and health. Physicians in America should never forget their responsibilities to all humanity or neglect their opportunities to promote the brotherhood of man.

We physicians have a unique opportunity to provide a spark of leadership which can help bring the world closer to the dream of world brotherhood. If you do not feel the compulsion of that task, I can only remind you of the Sputniks, Explorers, and Vanguards whirling overhead. They in themselves are but the toys of grown men, compared with the potential engines of destruction which put them into orbit. If our alternative is destruction or a dream, the only sensible choice is to make the dream work.

Medicine can play a vitally effective part in bringing reality to the dream of world peace. For medicine, despite the designs of politicians or dictators, is above the harsh conflicts of ideologies and power politics. Medicine, like religion, speaks a universal language which passes all barriers of race, creed, color, and nationality. Already, great work has been accomplished by individuals, private organizations, medical associations, and official agencies. In fact, the brightest chapter in the international story since World War II is that on health and medicine. This is no uncharted course; the way is well marked.

San Francisco is a particularly appropriate place in which to stress the challenge of international cooperation. For it was here in 1945 that the United Nations was formed and the first suggestion was made for establishment of a new international health organization. Three years later the World Health Organization came into being.

While the World Health Organization was going through its formative stages, the physicians of many countries were meeting informally to discuss the need for an international medical organization. As a result, the World Medical Association was officially established in September, 1947, with the American Medical Association as a founding member.

Thus, both organizations—rooted in postwar ideals of world collaboration—have just recently completed their first decade of service. From the beginning, they have maintained close liaison with one another and with many additional international groups interested in various phases of medicine, health, and general welfare. They are the main avenues for mobilizing and coordinating world medical resources for the common good of humanity.

Whereas the World Health Organization represents governments and the field of public health, the World Medical Association speaks for the medical profession. It now is composed of 53 national medical associations representing about half a million physicians throughout the world. Its principal objectives are to maintain the standards, ethics, and traditions of medical practice; to raise the standards of medical education; to promote the mutual exchange of information and ideas among the physicians of the world; to help raise the level of world health; and to promote world peace.

In pursuit of those objectives, the World Medical Association has carried out a wide variety of activities. As just one example, in 1953 the World Medical Association sponsored the First World Conference on Medical Education. More than 600 participants from over 60 countries and 127 universities and medical schools attended that London meeting, which focused attention on undergraduate medical education. The proceedings have been widely distributed throughout the world. The Second World Conference on Medical Education—spotlighting the theme of "Medicine as a Life-long Study"—will be held next year in Chicago, where we of the American Medical Association will be hosts to our medical colleagues from other lands.

Another new avenue of approach to help the cause of international peace is the Medicine and Health Professions Committee of the People-to-People Program, initiated last year by President Eisenhower. This program is designed to promote close contacts and friendships among individuals and groups who share professional, cultural, and economic interests. It is based on the idea that if the people of the world could begin to know one another—to meet, talk, correspond, and exchange visits—many of the world's troubles would be over. We might then begin to use the knowledge of the atomic age for humanity, rather than in an attempt to destroy our civilization.

American doctors, medical missionaries, nurses, and technicians—serving humanity in far flung parts of the world—are contributing immeasurably to this great cause. The work of some of them was beautifully reported last January in the March of Medicine telecast called "M.D. International." They were described as unofficial American ambassadors of good will—men and women who are demonstrating the forceful good that lies in the basic brotherhood of man, who are revealing our greatest hope for the future—man's humanity to man.

President Eisenhower recently pointed out that the armed forces of the United States are only supports for the much larger purpose of a just peace and the advancement of human well-being at home and throughout the world. In the struggle for peace, he said, "the strength that endures rests with those who live in freedom." And he added that "tyranny is too brittle—too insecurely based—too dependent upon force and brutality—too contrary to the hopes and ideals of humanity—to last over the long pull."

Physicians, alerted here and abroad, can do much to advance the cause of freedom and human well-being. For medicine, by its very nature, speaks a universal language dedicated to scientific truth, humanitarian service, individual dignity, and world peace. In medical science there are no secrets, no iron curtains, no cold war. To physicians everywhere, atomic energy means a new way of fighting disease, not a new way of conquering the world. Medicine exists to save life, not destroy it.

The demands of these troubled times require that we perform at only one level—our very best. The time has come for medical statesmanship which will help point the way toward better health—and a better life—for all the peoples of the world.

J.A.M.A., June 28, 1958

TREATMENT OF THE DUMPING SYNDROME

George L. Jordan Jr., M.D., Houston, Texas

It is important to recognize that the actual incidence of the dumping syndrome is high in the untreated patient, for by proper dietary management in the early postgastrectomy period these symptoms can be prevented, so only a small percentage of patients need ever have any significant difficulty. The ideal treatment for this syndrome would be prevention, and various techniques of gastrectomy have been advocated by different authors to produce a low incidence, but no technique has been uniformly successful in the hands of all investigators. Approximately one-half of the patients with mild symptoms desired no treatment at all, and most of the remainder were satisfactorily managed by diet or postprandial recumbency. None of the patients classified as having severe symptoms could be managed by diet or by the combination of diet and recumbency; however, the condition of several of these patients was improved by the use of antispasmodics and by blood transfusions.

The dumping syndrome is a complex physiological response to the presence of undigested food in the jejunum. The ideal therapeutic approach must await further investigation, for all of the factors involved in the pathogenesis of this syndrome have not been clearly defined. Nevertheless, therapeutic regimens based upon an understanding of pathophysiological alterations now delineated may relieve symptoms.

Diet

There is general consensus that dietary management is the basic factor in treatment.[1] Proteins are tolerated better than carbohydrates and solid foods better than liquids, for carbohydrates are hydrolyzed into osmotically active substances more rapidly than are proteins, and foods in the liquid state enter the jejunum rapidly. Studies of the effect of fat in the diet have not given consistent results, but there is some evidence to indicate that the form in which fat is administered may influence the production of symptoms. Thus, homogenized fats, particularly those fat solutions containing carbohyrates, are more likely to produce symptoms than are those fats of large molecular weight in the naturally occurring state.[2] Emptying of the gastric remnant is not dependent upon gastric peristalsis.[3] Therefore, administration of fat does not improve symptoms by slowing passage of food into the jejunum.

With these facts in mind, one should take a careful dietary history. Symptoms may occur after the ingestion of specific foods; such foods should be eliminated from the diet. For patients with symptoms more difficult to control, a strict dietary regimen should be outlined, consisting of six small daily feedings, high in protein, low in carbohydrate, and containing a moderate amount of fat. Milk is poorly tolerated by many postgastrectomy patients; consequently, it should be eliminated from the diet, as should ice cream, milk shakes, pies, and other sweets. Each meal should be eaten dry, and fluids taken between meals should contain a minimal amount of sugar or none at all. A dietary regimen of this type may give satisfactory relief in many patients. Robinson and Pittman [1c] found that complete or partial relief was obtained in 80% of patients studied.

Postprandial Recumbency

Those patients who need additional help may lie down for 20 to 30 minutes in the immediate postprandial period. Amdrup [4] found that the injection of stimulating foods directly into the jejunum caused symptoms, regardless of posture, but when foods were taken orally symptoms were less if the patients was recumbent. Roentgenographic studies demonstrate that gastric emptying is slower when the patient is in a recumbent position, and this appears to be the primary effect of this maneuver.[3] Unfortunately, many patients do not always have access to a bed after meals.

Antispasmodics

The most extensive study of the use of antispasmodics was reported by Rauch and Bieter,[5] who investigated a number of drugs and found that atropine was rarely beneficial, whereas methantheline (Banthine) bromide relieved 26% of the group. An experimental drug produced complete relief in 35% of the patients treated, but unfortunately it resulted in so many undesirable side-effects that clinical use on a large scale was not practical. These authors found that β-diethylaminoethyl 9-fluorenecarboxylate hydrochloride (Pavatrine) was the most effective drug, free of side-reactions, giving complete relief in 22% and partial relief in 30% of the patients. Capper and Welbourn [6] state that drugs have proved disappointing. These authors used hexamethonium bromide, hoping to block the autonomic ganglions and reduce visceral sensation. Studies in this clinic indicate that the effect of antispasmodics is primarily that of decreasing jejunal motility, thereby decreasing the speed of gastric emptying as well as decreasing nausea, vomiting, and diarrhea.[2a] Since most of the antispasmodics have an anticholinergic action, they may also be of value in decreasing the

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passage of fluid into the gastrointestinal tract, though this latter action has not been demonstrated objectively.

When utilizing antispasmodic drugs, it is important to realize that the response in the fasting state is quite different from the response in the postprandial state and that the response of a given individual to various antispasmodics differs. By trial and error one may establish the drug which produces the maximum effect. In clinical practice, it is desirable to start therapy with a drug which has minimal side-effects, for dryness of the mouth, blurring of vision, or urinary retention may be as distressing to the patient as his dumping symptoms. A drug may be administered empirically for a period of one to two weeks and the effect assessed. If the patient obtains a good result, it is quite likely that this effect will be persistent. If the first drug tried does not produce symptomatic relief, additional drugs should be employed until the proper one is found, for failure to respond to one drug does not preclude an excellent response to another. An occasional patient will have complete control with administration of the drug alone; however, dietary measures will also be required in most patients. Failure to obtain control of symptoms with a combination of diet, antispasmodics, and postprandial recumbency is rare except in patients with very severe symptoms.

Blood Volume Replacement

Since the work of Roberts and her associates,[7] other investigators [8] have confirmed the finding of a decrease in blood volume in the immediate postprandial period, which coincides well with the symptomatic period. Many observers feel that this alteration is of significance in production of vasomotor symptoms, though it is probably not as important as first believed.

Most patients with this syndrome have a normal blood volume; however, a few patients have a depleted blood volume resulting from inadequate nutrition, and this may impair their ability to withstand these postprandial hemodynamic changes. Therefore, the blood volume should be determined in those patients who fail to respond to the measures already mentioned, for restoration to normal may result in significant symptomatic improvement and convert an intractable condition to one managed satisfactorily by diet or antispasmodics.[9]

Potassium Salts

On the basis of electrocardiographic changes occurring in the postprandial period, Smith [10] suggested that acute alterations in serum potassium concentration might play a role in symptom production, and Kleiman and Grant [11] reported good results with the use of potassium salts clinically. There is some evidence to indicate an inverse relationship between the magnitude of fall in the serum potassium concentration and the fall in blood volume during the symptomatic period.[8] Therefore, the role of potassium changes in the production of symptoms is not completely settled, but in the minds of most investigators alterations in serum potassium concentrations are of little or no significance. From a clinical standpoint, the good results reported by Kleiman and Grant have not been duplicated by others.[6]

Psychotherapy

There are those who maintain that this syndrome is primarily functional in origin and that many patients may be successfully treated by psychotherapy.[12] Some postgastrectomy patients have psychoneurotic symptoms which may be confused with the dumping syndrome; and some patients who have the dumping syndrome will, in addition, have psychoneurotic tendencies which make management of their problem more difficult. Certainly many of these patients will be improved by psychotherapy, and in most instances the physician in charge of the patient will be able to accomplish this. In addition, reassurance that the symptoms do not signify a serious disorder will relieve anxiety in many patients. Nevertheless, the weight of evidence which has been accumulated in the past years leaves little doubt that the dumping syndrome, as described herein, is the result of physiological abnormalities, and, therefore, psychotherapy should be used as a therapeutic adjunct rather than the primary approach to treatment.[13]

Leonard and his associates [14] have recently reported the use of hypnosis to control severe symptoms in some patients. We have had no experience with this procedure, but its use may be justified in those patients with intractable symptoms.

Other Nonoperative Measures

Welbourn states that Kay regards the administration of an oral local anesthetic, such as procaine hydrochloride, a valuable therapeutic measure, but he was unable to verify these observations.[6] Glazebrook and Wrigley state that symptoms have been relieved in some patients by the administration of sodium bicarbonate, and Capper and Welbourn [6] have noted similar results. We have administered this drug occasionally without success. Butler treated 61 patients by paravertebral injection of procaine hydrochloride and obtained relief in 50 of these. Improvement in symptoms was transitory in most, but in four the effect appeared permanent, as no symptoms had returned after several months.[15]

Surgery

Each of the measures noted above should be attempted before surgical intervention is considered, but the few patients who fail to respond may obtain some relief through operative modification of their gastrointestinal anastomosis. This subject has been extensively reviewed by Capper and Welbourn,[6] who collected 14 patients treated by support of the lesser curvature and afferent loop, with 79% relief; 9 patients with jejunal replacement had 100% relief; 30 patients with colonic replacement had 80% relief; and 63 having conversion to Billroth 1 anastomosis had 84% relief. Unfortunately the follow-up period is short in all of the reported cases; therefore, the high incidence of symptomatic improvement must be accepted with some reservations. All but one of these procedures is basically a conversion to the Billroth 1 anastomosis.

Other procedures which have been advocated include jejunoplasty, narrowing of the gastroenteric stoma, vagotomy, and splanchnicectomy. The evidence to date indicates that the procedure of choice is conversion to a gastroduodenostomy, if gastrojejunostomy was originally performed. There is no good evidence to indicate that surgical modification of a gastroduodenostomy is likely to be beneficial. This study was undertaken to assess the therapeutic results obtained in our clinic.

Materials and Methods

The records of 400 patients treated by subtotal gastrectomy were reviewed. Of this group, there were 300 (75%) with duodenal ulcers, 60 (15%) with gastric ulcers, 14 (3%) with gastrojejunal ulcers, 4 (1%) with gastritis and hemorrhage, and 22 (6%) with carcinoma. Of these patients, 144 (36%) experienced symptoms typical of the dumping syndrome. The symptoms uniformly appeared during the meal or within 10 to 20 minutes after ingestion, and were characterized by nausea, with or without vomiting, and occasionally diarrhea, as well as a vasomotor component of weakness, sweating, pallor, and/or increased pulse rate.

TABLE 1.—*Methods of Treating Patients with Dumping Syndrome*

	Patients with Mild Symptoms		Patients with Moderate Symptoms	
Treatment	No.	%	No.	%
None	34	48	8	12
Diet	27	38	17	27
Postprandial recumbency	6	8	1	2
Antispasmodics	2	3	31	48
(Lost to follow-up)	2	3	7	11
Total	71	100	64	100

Symptoms were classified as mild if they occurred only after a very large meal, were of little concern to the patient, or occurred only after the eating of specific foods which could easily be eliminated from the diet. If symptoms occurred once or twice weekly, despite attempts by the patient to obtain relief, they were deemed moderate. Symptoms were classified as severe when they occurred after almost every meal and were incapacitating to the point of interfering with normal activity. There were 71 patients with mild symptoms, 64 with moderate symptoms, and 9 with severe symptoms. (These represented 18, 16, and 2% of the total group and 50, 44, and 6% of the group with dumping syndrome.)

All of the patients with severe symptoms and approximately one-half of those with moderate symptoms underwent specific diagnostic studies (electrocardiography, studies of blood volume, jejunal motility, serum potassium concentration, and/or efferent loop aspiration) to confirm the diagnosis objectively and to exclude other postgastrectomy syndromes as the cause of symptoms. One-hundred thirty-four patients (93%) were followed for periods of six months to four years after the onset of symptoms.

Treatment and Results

Approximately one-half of the patients with mild symptoms desired no treatment at all, and most of the remainder were satisfactorily managed by diet or postprandial recumbency. Only two required antispasmodics in their therapeutic regimen (table 1.) It was possible to obtain complete relief of symptoms in each of these patients.

Of the patients classified as having moderate symptoms, eight desired no treatment and preferred to eat as they liked and experience symptoms occasionally rather than employ a therapeutic regimen. Only one patient obtained satisfactory control by postprandial recumbency alone, though there were six additional patients who utilized this maneuver in combination with dietary control. Almost one-half of these patients required antispasmodics as an aid in symptom control (table 1). Of the 49 patients who desired treatment and who were followed, complete relief of symptoms was obtained in 37% and partial relief in 55%. Of the four patients (8%) who failed to respond to the various regimens employed, one had complete spontaneous relief after a period of two years, one was not properly treated, and the remaining two patients did not desire further attempts at therapy.

None of the patients classified as having severe symptoms could be managed by diet or by the combination of diet and recumbency. Two patients obtained complete relief of symptoms when antispasmodics were added to the regimen, and one obtained partial relief, so that additional measures were not necessary. The remaining five patients failed to respond. One patient subsequently had spontaneous regression so that no further attempts at therapy were indicated. A jejunal pouch was created in two patients. One had partial relief of symptoms for approximately a year, after which time symptoms recurred as severe as they had been previously, while the other patient experienced no relief at any time. The patient obtaining partial relief of symptoms for a short time following operative intervention was subsequently proved to have a low blood volume, and correction of blood volume to normal allowed satisfactory control with diet alone. At the present time he has been followed for 18 months since correction of his blood volume deficit and has done well. The normal blood volume has been maintained.[9]

Of the remaining two patients, one has a severe psychiatric problem in addition to his dumping syndrome, which makes control virtually impossible, while the second patient feels that an attempt to stay on a strict regimen interferes with his daily activities more than does his symptomatology. He is an aggressive, active businessman who works long hours daily, despite his dumping symptoms. One patient was not traced.

Orally given anesthetics, sodium bicarbonate, paravertebral block, and orally given potassium salts have each been tried. Our experience with these agents is too limited to warrant definitive evaluation, but no patient obtained relief of symptoms. Of the 92 patients who desired treatment, in the early follow-up period 55 (60%) obtained complete relief of symptoms, 29 (31%) obtained partial relief, and 8 (9%) obtained no relief. There were no patients who subsequently became refractory to treatment after having an early good result, but 17 patients (13%) had spontaneous improvement, so that with the passage of time the number of patients with complete relief of symptoms increased. Thus, at the present time 67% of the treated group have complete relief, while only 6% have failed to improve. These six patients represent only 1.5% of the entire group of 400 postgastrectomy patients. Four of these patients have continued to work despite their symptomatology and have not required hospitalization, while two are totally incapacitated.

Comment

The reported incidence of the dumping syndrome varies from 2 to 45%.[16] In all probability much of the difference in incidence reported depends upon the definition of dumping and the detail with which the history was taken. Thus, those patients who can prevent symptoms simply by eliminating offending foods may be listed as having a food intolerance rather than the dumping syndrome. Some authors have classified patients as having the dumping syndrome only if the symptoms were incapacitating. Furthermore, by taking a careful history one finds many patients who deny symptoms except on detailed questioning.

It is important to recognize that the actual incidence of the syndrome is high in the untreated patient, for by proper dietary management in the early postgastrectomy period these symptoms can be prevented, so only a small [illegible] of patients need ever have any [illegible]. Our experience indicates that approximately 15% of patients treated by subtotal gastrectomy *may need* help in alleviation of symptoms. This can be accomplished with patience, reassurance, and proper selection of a therapeutic regimen. Several weeks may be required to establish satisfactorily the best therapeutic regimen for an individual patient. The response to a specific antispasmodic varies from patient to patient, and it may be necessary to try several before the one producing the optimum results is found.

Fortunately, those antispasmodics with the least number of side-effects are as effective as those producing a greater number of side-effects (table 2). All of our patients who obtained complete relief for as long as two to three weeks with the use of antispasmodics have continued to obtain good relief with the use of such drugs for follow-up periods of as long as three years. Once the use of an antispasmodic is necessary, most patients will require its use indefinitely if symptoms are to be controlled.

The ideal treatment for this syndrome would be prevention, and various techniques of gastrectomy have been advocated by different authors to produce a low incidence, but no technique has been uniformly successful in the hands of all investigators. In our patients the Billroth 1 and Billroth 2 procedures were used, as well as jejunoplasty. The total incidence of postgastrectomy symptoms does not appear to be greatly different when the Billroth 1 and Billroth 2 procedures are compared, but only one of the patients with severe symptoms was treated by the Billroth 1 procedure, and this patient was the one who eventually had spontaneous remission of symptoms.

Thus, our observations tend to support those of Capper and Welbourn,[6] who found that the incidence of severe symptoms was lower following gastroduodenostomy. Unfortunately, this procedure is attended by such a high incidence of marginal ulcer when used in the treatment of duodenal ulcer that it cannot be recommended. However, we consider gastrectomy with gastroduodenostomy the treatment of choice for gastric ulcer, since the incidence of marginal ulceration is low following surgical management of this lesion. It is our belief that patients treated for gastric ulceration are less likely to develop this postgastrectomy syndrome than are patients treated for duodenal ulceration, regardless of the surgical procedure employed. It is noteworthy that no patient treated for gastric ulcer developed severe postgastrectomy symptoms.

TABLE 2.—*Results Obtained with Antispasmodic Drugs in Treatment of Dumping Syndrome*

Drug	Patients, No	Incidence of Symptoms of Relief, %		
		None	Partial	Complete
β-Diethylaminoethyl 9-fluoroenecarboxylate hydrochloride (Pavatrine)	3	100	0	0
Mixture of Dactil and Piptal, 10:1 (Tridal)	2	50	50	0
Pipenzolate methylbromide (Piptal)	10	40	50	10
Methantheline (Banthine) bromide	8	74	13	13
Hexamethonium bromide	12	42	42	16
Belladonna	14	36	43	21
Piperidolate hydrochloride (Dactil)	20	35	30	35

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METASTATIC TESTICULAR TUMOR TREATED WITH NITROFURAZONE

REPORT OF A CASE

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A testicular teratocarcinoma occurring in a 35-year-old man was treated initially by surgery and later by irradiation of the inguinal and abdominal regions. Chest films showed an initial absence of pulmonary metastases, but later films showed the gradual appearance of pulmonary lesions until, six months after operation, 12 or 13 such lesions were visible. Administration of nitrofurazone in doses of 0.5 Gm. twice (later three times) a day by mouth was followed by the complete disappearance of some of these nodules. The onset of a severe peripheral neuritis made it necessary to discontinue this treatment. Symptoms of pulmonary involvement recurred, and the chest films revealed an increase in the size and number of the lesions. The patient died of metastases to lungs, liver, brain, pericardium, and regional lymph nodes. This history closely parallels reports by other authors as to the striking therapeutic effects as well as the painful side-effects of nitrofurazone, and indicates the importance of further trials of this drug and its derivatives.

Nitrofurazone (Furacin) has been used perorally in several cases of human seminoma and embryonal carcinoma.[1] In 1952 Friedgood and associates[2] reported four cases of testicular seminoma treated with nitrofurazone. In all of these, there was marked degeneration of the tumor cells, increased fibrosis, and decreased cellularity of the tumor. In 1955, Wildermuth[1b] reported a case of testicular cancer treated with nitrofurazone. The patient had developed widespread pulmonary metastases after a complete course of postorchiectomy irradiation. Nitrofurazone was administered orally, 1.5 Gm. daily for two weeks and then 2 Gm. daily for two more weeks. The patient developed a severe painful peripheral neuropathy, and nitrofurazone was withdrawn. Three weeks later the neuritis improved slightly, but roentgenographically the improvement of pulmonary lesions was so marked that administration of 1.5 Gm. of nitrofurazone a day was started again and continued for one week, when the neuritic pain again became unbearable. The patient's chest film taken on Jan. 21, 1955, was free of recurrences (though pulmonary scars persisted), and he was able to work a full eight-hour day. The patient died in October, 1955, of cerebral metastases, with a survival period of over two years. Another patient was treated but could not tolerate the drug.

The purpose of this paper is to report an additional case of testicular carcinoma with striking temporary decrease of multiple pulmonary metastases after nitrofurazone therapy.

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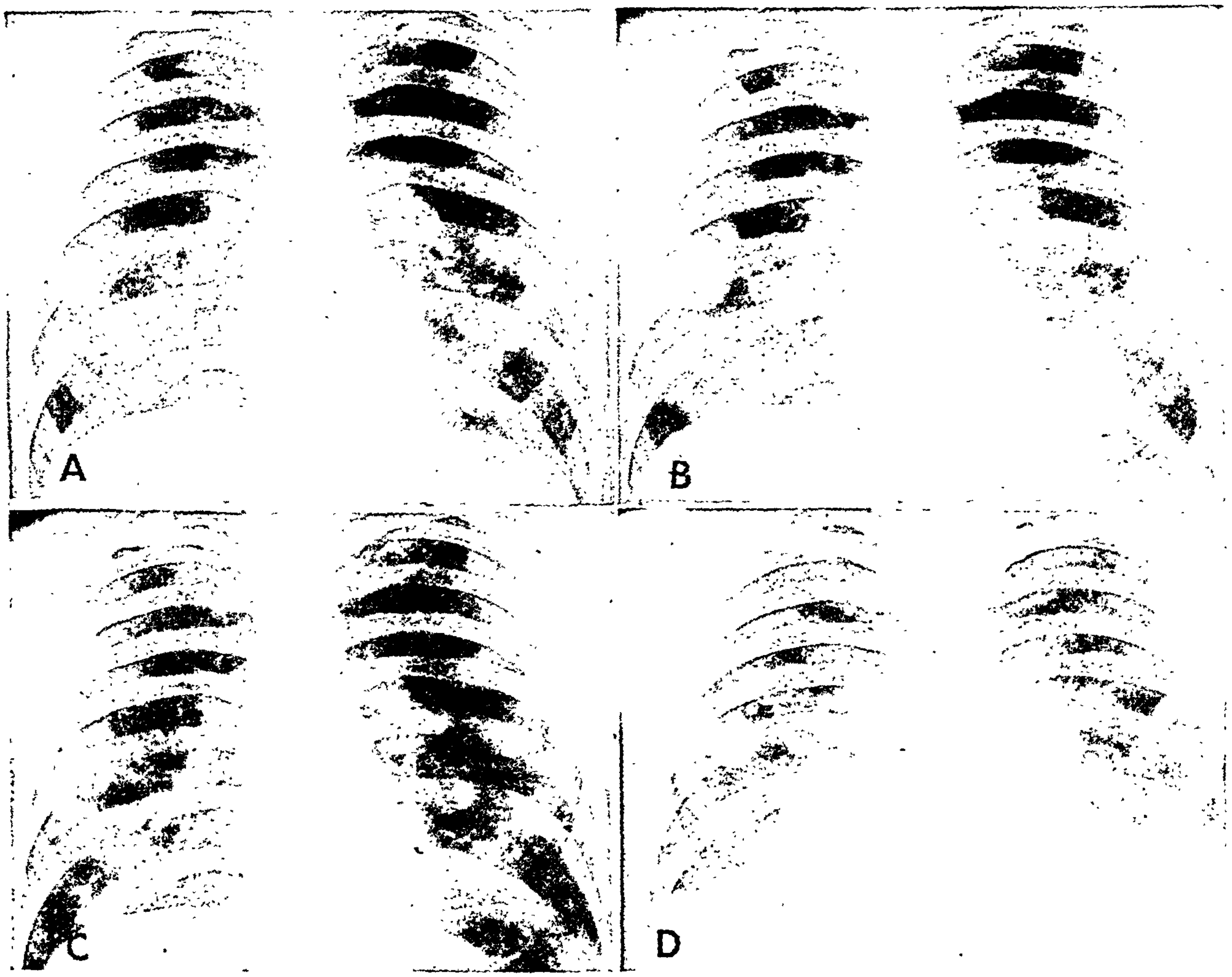
A 35-year-old man was transferred to the Denver Veterans Administration Hospital on April 18, 1955. He gave a history of having noted an increase in the size and firmness of the right testis for the first time in January, 1955. Some weeks later a small, nodular, tender mass appeared in the right inguinal region. The history was not remarkable except for a right inguinal herniorrhaphy and orchiopexy 18 years previously.

On March 14, 1955, the right testis and right inguinal mass had been removed at the Cheyenne VA Hospital. The histological diagnosis was teratocarcinoma involving the testis and lymph node. Ten days later a radical inguinal femoral and retroperitoneal node dissection was done on the right side. Several of the nodes were found to be involved with metastatic cancer. A chest film revealed no metastases.

Physical examination on admission revealed a well-developed, well-nourished male in no distress. The positive physical findings consisted of a large, infected ulcer of the right groin, tenderness along the course of the saphenous vein, a well-healed surgical scar of the right abdomen, and absent right testis. The heart and lungs revealed no abnormalities and there was no lymph node enlargement. Laboratory tests on admission revealed a normal urine, a hemoglobin level of 15.5 Gm. per 100 cc., and a white blood cell count of 6,300, with a normal differential count. No chest or bone metastases were found at this time.

The patient was given heparin and bishydroxycoumarin (Dicumarol), and the saphenous thrombophlebitis subsided in four days. He was then given abdominal (para-aortic) radiation with 1,000 kv. (3,000 r tumor dose). The right inguinal region was treated with 250 kv. (3,000 r in air). This x-ray therapy was carried out between May 14 and Aug. 1, 1955. On the latter date a chest x-ray showed a small ovoid density in each lung. The frog test for urinary gonadotropins was negative on Aug. 5. The patient was discharged two days later, to be followed as an outpatient by the tumor clinic. A follow-up x-ray on Oct. 4 revealed 12 or 13 soft ovoid densities (0.5 to 3 cm.) scattered throughout both lung fields (see figure, A).

The patient was readmitted on Nov. 28, 1955, for treatment with nitrofurazone, which was administered perorally in a dose of 0.5 Gm. twice a day from Dec. 1 to Dec. 12 (12 Gm. total). A chest film on Dec. 12 showed an increase in the size of the pulmonary lesions (see figure, B). The next day a small intestine obstruction developed and was relieved surgically by Nobel plication. Nitrofurazone therapy (0.5 Gm. twice a day) was resumed on Dec. 28 and continued until Jan. 6, 1956, when the dose was increased to 0.5 Gm. three times a day until Jan. 15 when the drug was withdrawn. The total dose administered during this period was 35 Gm. [illegible] ...ic symptoms referable to the [illegible] ...d nausea and vomiting until



Chest roentgenograms. *A*, Oct. 4, 1955, before nitrofurazone therapy, revealing multiple round metastatic lesions scattered throughout lung fields and hilar areas. *B*, Dec. 12, 1955, showing increase in size of pulmonary lesions. Nitrofurazone therapy was started Dec. 1. *C*, Feb. 24, 1956, revealing maximum regression of metastases. Several lesions disappeared completely. Nitrofurazone therapy (35 Gm.) was completed Jan. 15. *D*, Aug. 28, 1956, showing innumerable metastatic nodules of various sizes scattered throughout lungs. Note that original lesions never increased to pretreatment size.

Jan. 14, when the patient developed severe peripheral neuritis which persisted for approximately two and one-half months and required heavy doses of narcotics for control of pain. During this period his general condition deteriorated. When the neuritis subsided, he improved markedly.

The frog test was positive on Nov. 29, 1955, before nitrofurazone therapy, but negative on Jan. 13, 1956, after administration of 33 Gm. of nitrofurazone. A chest film taken Dec. 18 showed no change in the pulmonary metastases from that of Dec. 12 (see figure, *B*), but the film obtained on Jan. 18 revealed a decrease in the density and size of several of the lesions. A film taken Feb. 24 (see figure, *C*) showed further regression in the size and density of many of the lesions, with complete disappearance of several small ones and nearly complete disappearance of a 3.5-cm. nodule in the left lower lung field. There remained only a 2.5-cm. lesion on the right and two or three smaller lesions on the left. On March 23 the lung lesions appeared to be slightly larger, and progressive enlargement of a supraclavicular node was noted. However, the patient's general condition was considerably improved and he was discharged from the hospital on April 9, 1956.

The patient was readmitted on May 9 for follow-up evaluation. Since his previous discharge, he had traveled extensively and felt well. His weight had remained constant and he had noted no gynecomastia. His only complaint was mild discomfort in the right side of his chest. A chest film on admission showed the lung metastases to be larger and slightly denser, and a frog test was positive again. Retreatment with nitrofurazone was deferred because of the severe peripheral neuritis which occurred with previous administration of the drug. The patient was discharged on May 23.

The patient was readmitted on Aug. 13, 1956, because of dyspnea, peripheral edema, bilateral chest pain, hemoptysis, and a large tender mass in the left upper part of the abdomen. A chest film taken on Aug. 28 (see figure, *D*) revealed an increase in the number and size of the metastases. The patient's condition deteriorated rapidly and on Sept. 8 hemiparesis on the left side developed. Death occurred on Sept. 12, 1956. Autopsy revealed metastases to the lungs, liver, pericardium, and regional lymph nodes. There was a massive hemorrhage of the right cerebral hemisphere, but no tumor mass.

Comment

The nitrofurans are a group of synthetic organic chemicals whose antibacterial effectiveness was first reported in 1944.[3] Over 450 nitrofurans have been synthesized, the best known being nitrofurazone (Furacin), used mainly as a topical antibacterial agent, and nitrofurantoin (Furadantin), used perorally for treatment of genitourinary tract infections and intravenously for systemic infections. Nitrofurazone was reported to delay the growth of certain experimental mouse tumors in 1948.[4] Other studies established that certain nitrofurans block spermatogenesis in rodents [5] and in man.[1c] Nitrofurazone arrests spermatogenesis at the primary spermatocyte level and causes degenerative changes in mature spermatozoa, spermatids, and secondary spermatocytes. Primary spermatocytes become rare but never disappear entirely. The spermatogonia and Sertoli cells are unaffected. The Leydig cells and androgen production remain unchanged. Recovery of the testis starts on about the sixth posttreatment day and is complete in about six weeks.

Chronic overdoses of these compounds in mice, rats, and dogs cause slight adrenocortical hypertrophy. The earliest symptoms of toxicity are nausea and vomiting, apparently due to both central and local actions. At higher dose levels neurotoxic symptoms occur. The acute oral LD_{50} of nitrofurazone in mice is from 380 to 735 mg. per kilogram of body weight.[6] Several reports indicate that orally administered nitrofurazone is safe in man at doses of 0.5 to 2.0 Gm. per day.[1] The principal toxic reactions in man have been nausea, vomiting, and severe peripheral neuritis. Chlorpromazine and enteric-coated tablets may relieve the nausea and vomiting. Narcotics, in addition to general supportive measures, may be required to control the neuritis. The dose of nitrofurazone is determined by the tolerance of the patient. In general, a daily dose of 1.25 to 2 Gm. in three or four divided doses has been used.[1b]

Summary and Conclusions

A 35-year-old patient with a teratocarcinoma of the testis developed pulmonary metastases after orchiectomy, radical retroperitoneal node dissection, and x-ray therapy. Nitrofurazone (Furacin) was administered perorally to a total dose of 35 Gm. over a period of six weeks. The pulmonary metastases decreased markedly in number and size for a period of several months. The clinical response was difficult to evaluate owing to the occurrence of a severe peripheral neuritis. Death with recurrent pulmonary metastases and cerebral hemorrhage occurred nine months after the course of nitrofurazone.

It is concluded that nitrofurazone should be given further trial in the treatment of testicular tumors. This drug may also be useful preoperatively and in conjunction with irradiation to control or eradicate metastases of testicular tumors.

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The *nitrofurazone* used in this study was supplied as Furacin by the Eaton Laboratories, Norwich, N. Y.

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FARMER'S LUNG

AN ACUTE GRANULOMATOUS INTERSTITIAL PNEUMONITIS OCCURRING IN AGRICULTURAL WORKERS

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Farmer's lung is a potentially serious and crippling disease that results from handling a variety of dusty, moldy organic materials. The symptoms are shortness of breath, cough, fever, chills, weight loss, and hemoptysis. This condition differs from silo filler's disease in both causation and symptoms. The roentgenographic findings are those of interstitial pneumonitis. Biopsy of the lung reveals a granulomatous interstitial pneumonitis with epithelioid and giant cells. This report is based on 39 cases. Lung biopsies were done in eight, and two cases are described in detail. Repeated exposure was followed by recurrence. No causative organism was found. A given exposure induced the disease in some persons while leaving others unaffected. Individual hypersensitivity to molds or to their products seemed to be a decisive factor. Antibiotic therapy is not primarily indicated. The essential treatment is for the patient to avoid repetition of the exposure.

During the past several years, we have encountered, with increasing frequency, a peculiar respiratory illness among farmers who have been exposed to moldy forage. This disease is a distinct, easily recognized clinical syndrome with uniform clinical, roentgenographic, physiological, and pathological features. It is, we believe, an important hazard to agricultural workers, which is not related to the recently described, superficially similar, but much less frequently encountered silo-filler's disease.[1] The purpose of this report is to document the major features of this syndrome so that it may receive the attention which we believe it deserves.

During the past eight years, 36 men and 1 woman have been seen at the University Hospitals and 2 additional men have been seen at the Madison Veteran's Administration Hospital on account of respiratory difficulties of varying severity. The duration of symptoms varied from three days to 10 years, but the average patient had had recurrent difficulties for approximately 3 years. All had received prior medical attention, and one-half had been hospitalized elsewhere one or more times. Their ages varied from 12 to 65 years. Two were between 10 and 20 years of age, 6 between 21 and 30, 9 between 31 and 40, 10 between 41 and 50, 10 between 51 and 60, and 2 between 61 and 70. All but two were life-long farmers, and it seems clear that the disease appeared only after many years of farming experience.

The onset of the acute illness followed exposure to various dusty jobs on the farm. Only two individuals were uncertain about the presence of mold in the dust thought to be responsible for the attack. The type of dusty material handled by others prior to the onset of their first acute episode included moldy hay, fodder, and grain, 19; moldy silage, 11; moldy shredding or threshing dusts, 6; and moldy tobacco, 1. Moldy hay, grain, fodder, and silage were thus the most frequent offenders, while the dusty atmosphere associated with threshing and shredding was also felt to be an offending agent. Exposure usually occurred within a closed bin, silo, or barn where ventilation was poor.

Clinical Features and Laboratory Findings

Clinical Features.—In most instances, exposure to a dusty job was followed within a few hours by chills, fever, cough, and shortness of breath. A few patients had experienced some minor symptoms, such as chills, headache, or malaise, when in contact with the offending dusts prior to the exposure which produced the alarming respiratory difficulty.

The major symptoms of the entire group were as follows: Shortness of breath was a constant complaint (39, or 100%). This was noted by most of the affected individuals during the acute febrile episode. In some, there was alarming dyspnea, frequently associated with cyanosis. More commonly, the patient's original illness was such that the acute malaise, fever, and chills were more striking, and only when this acute episode subsided and the farmer attempted to return to his ordinary farm work did he realize that he became very short of breath on the slightest exertion. This sharp limitation of ability to perform work persisted for several weeks after an acute febrile episode. Cough

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was present in all but a 12-year-old boy (38, or 97%). The cough was a harassing one which occurred at the onset of the acute illness and persisted for several days without the patient having further contact with the moldy material. The chronicity of the cough, as well as other symptoms, was frequently difficult to determine because the individual usually returned to the dusty environment. Fever was likewise a very common symptom (38, or 97%), and, in many individuals, actual temperature elevations to 104 to 106 F (40 to 41.1 C) were recorded. Associated with the fever was a generalized malaise and severe headache. Severe shaking chills were frequent (33, or 85%), as well as the less dramatic sensation of chilliness.

Weight loss of 10 to 20 lb. (4.5 to 9.1 kg.) was common in this group of men who usually were not overweight at the time of their illness (29, or 88%; not recorded in 6). The sputum was usually neither copious nor very purulent. Although two patients had experienced frank hemoptysis, the usual description of the bleeding episode was that of blood-streaked sputum (10, or 26%). Tightness of the chest was a common symptom, but a pleural type of pain was seen in only one individual, who developed cough fractures of the ribs. The patients were usually free of symptoms during the summer, when stored forage was not being used, but had recurrent difficulties during the winter months.

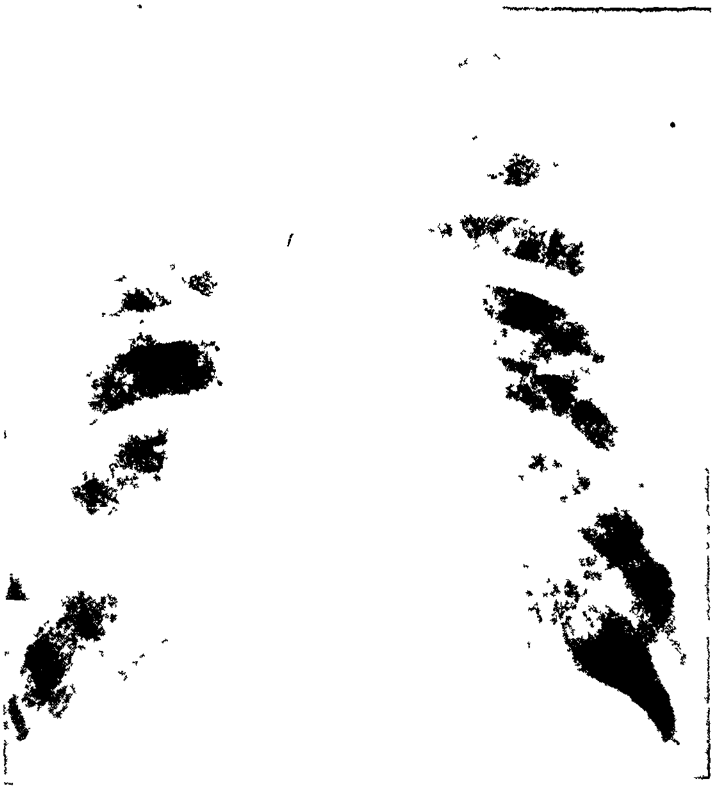

Fig. 1.—Chest roentgenogram showing most characteristic evidence of farmer's lung: interstitial pneumonitis.

In this type of illness, the problem of an allergic diathesis of the patient must be considered. A familial history of some recognized illness frequently associated with an allergic state was obtained in nine, or about one-fourth of the group. Only five patients gave any history of a previous illness suggesting an allergy. Three patients had previously had asthma and hay fever, and one had previously noted hay fever during the height of the ragweed season. Another patient suffered from "chronic sinusitis." All of the asthmatic patients were convinced that the type of shortness of breath, even in the acute episodes, was distinct from the respiratory distress they had previously noted in their asthmatic attacks.

The abnormalities that could be demonstrated on physical examination of these patients varied considerably, according to the severity of their illness. It was noteworthy that the acutely ill, frequently cyanotic, febrile patient did not appear as critically ill or suffering with as severe a toxic reaction as the usual patient with pneumonia who had a comparable degree of respiratory embarrassment and cyanosis. Numerous crepitant rales, without evidence of consolidation and without the wheezing and obvious expiratory effort noted in the patient with an acute asthmatic attack, was the usual finding. Breathing was shallow and rapid. These patients resisted anything that would increase the respiratory excursion, because of the severe cough that resulted. In the less severely ill patient, numerous fine crepitant rales at the end of a forced inspiration were the most constant finding. These rales persisted long after the chest roentgenogram had returned to a normal appearance. Forced expiration frequently resulted in the finding of a few high-pitched squeaks, suggesting involvement of the finer divisions of the bronchial tree.

Laboratory Findings.—Sputum examinations for fungi were done in 30 of the 39 patients. Of these, 16 patients' sputums revealed Candida albicans, 1 C. parakrusei, and 1 Aspergillus. An incidence of C. albicans in approximately 50% of the sputums in a group of patients who nearly all had previously had antibiotic therapy is of uncertain significance.

A polymorphonuclear leukocytosis, with counts varying from 11,000 to 22,000 per cubic millimeter, was found in 10 of the 39 patients. All were having an acute episode and were still febrile. Eosinophilia was observed in 6 of the 39 patients, and the eosinophil level varied from 5 to 16%. It is possible, too, that this eosinophilia was due to prior antibiotic therapy, especially that with streptomycin sulfate. Only five individuals revealed a slight increase in the total red blood cell count, hemoglobin level, and hematocrit value. This was so slight as to be of doubtful significance.

Chest Roentgenograms, Pulmonary Function Studies, and Pathology

Chest Roentgenograms.—The chest roentgenograms varied considerably with the severity and the duration of the illness. Extensive interstitial changes so marked that the radiologist suggested the diagnosis of an "azotemic lung" were seen in one acutely ill patient. The usual finding, however, was a diffuse interstitial pneumonitis with varying degrees of patchy pneumonic densities (fig. 1).

These more conglomerate densities tended to clear within a week or two, but peribronchial accentuation persisted for at least a month or even longer. In the more chronically involved patient who had repeated episodes, fibrotic stringy densities appeared and cleared slowly, if at all. Right pleural thickening of considerable degree developed in one patient who was followed for eight years. It is important to recognize that a normal appearance of the chest roentgenogram does not exclude the diagnosis of farmer's lung. Among the patients for whom lung biopsies were done, the immediately preoperative chest roentgenograms were interpreted as having returned to normal in two patients but the lung biopsies in both instances revealed an acute granulomatous interstitial pneumonitis. The complaints of dyspnea on exertion persisted after the roentgenographic evidence of an acute interstitial pneumonitis had disappeared.

Pulmonary Function Studies.—Space does not permit more than a brief summary of the physiological abnormalities that may be present. During the acute episode of pneumonitis, there may be severe hypoxia of arterial blood, which is the result of a striking reduction in pulmonary diffusing capacity and abnormality in the relationship of ventilation and pulmonary blood flow. When the patient is well enough to tolerate more extensive pulmonary function studies, there is found to be hyperinflation of the lungs with a significant increase in residual volume and functional residual capacity and a moderate reduction in vital capacity. The moderate reduction in maximum breathing capacity, timed vital capacity, and expiratory air flow rates confirm the clinical impression of obstruction in the small bronchi or bronchioles.

Pathology.—Surgical biopsies of the lung were done in eight patients. In six, the abnormality noted was an acute granulomatous interstitial pneumonitis consisting chiefly of epithelioid cells and a few giant cells. A few well-formed tubercles were present. In two patients, these changes were not seen. In one (case 2), the lesion was that of an interstitial fibrosis which was consistent with a history of repeated difficulties for eight years prior to the taking of this biopsy. In the other patient. the granular nodular densities had cleared almost completely. The only abnormality noted was fibrosis of the lung with patchy collections of lymphocytes. No epithelioid or giant cells were noted. This patient had a characteristic history and an interstitial pneumonitis, which cleared slowly. It is possible that the biopsy was made in an area previously involved, since he had a history of pneumonia in 1940 and the pleural space was obliterated by adhesions at the time of the surgical biopsy. The smears and cultures of these lung specimens did not reveal fungi or tubercle bacilli. There was no evidence of caseation necrosis noted in any of the specimens.

Report of Cases

Case 1.—A 22-year-old man, a farmer, was admitted April 23, 1956, because of cough and shortness of breath for one year. He had enjoyed excellent health until late in the spring of 1955, when he baled old hay which was covered with a white mold and was very dry and dusty. This work was done in the morning, and by that afternoon he noted shortness of breath, weakness, chills, fever, a tight feeling in his chest, and an irritating, nonproductive cough. He was hospitalized at his local hospital for four days and was treated with penicillin and sulfonamides because of the roentgenographic evidence of pneumonia. After one week, he was able to work and felt quite well.

On the morning of Aug. 20, 1955, he removed spoiled, moldy, grass silage which had been stored in the silo early in July, 1955. By that afternoon, he had symptoms entirely similar to those noted previously. He was hospitalized for nine days. The diagnosis was "virus pneumonia." During this illness, he lost about 20 lb. (9.1 kg.). By Sept. 15, 1955, he returned to work but observed dyspnea when doing any heavy work. On Jan. 1, 1956, he developed a "head cold," characterized by nasal discharge, malaise, slight fever, and headache. After one week, a cough which was productive of a small amount of "yellow phlegm" was noted, accompanied by shortness of breath and anorexia. Chills and fever were intermittent, and he did not seek medical attention until Feb. 1, 1956, when he was hospitalized and treated with antibiotics for pneumonia and bronchitis. After three days, he was discharged but never "felt up to par." Chills, fever, and night sweats continued. Dyspnea occurred on climbing one flight of stairs, and he complained of palpitation on exertion. He was hospitalized for eight days, was treated with tetracycline, and felt improved. When he returned to his work, he again experienced chills, fever, and night sweats. On closer questioning, it was evident that at the time of the recurrence of his symptoms on Jan. 1, 1956, he had again worked with the grass silage which had been handled prior to the episode on Aug. 20, 1955. Although his father had worked with the same silage, he had experienced no illness.

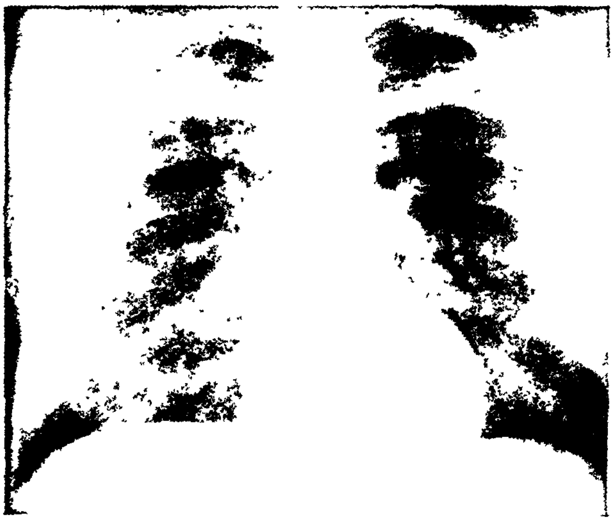

Fig. 2 (case 1).—Chest roentgenogram just prior to biopsy of lung.

The physical examination revealed a large, muscular young man who did not appear ill. A few fine inspiratory rales were heard at both bases. The chest roentgenogram (fig. 2) revealed minimal peribronchial changes. Chest roentgenograms taken in June, 1955, had shown minor interstitial changes. On March 2, 1956, there was a definite interstitial change most marked at the left lung base. This had cleared considerably by March 9, 1956. Biopsy of the lung revealed the characteristic granulomatous interstitial changes (fig. 3).

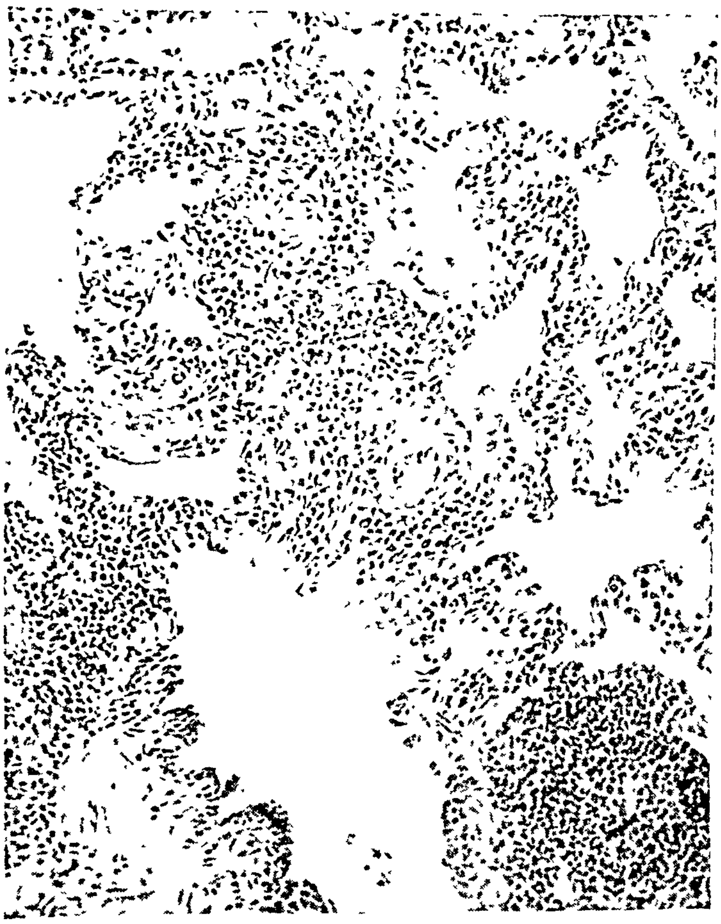

Fig. 3 (case 1).—Photomicrograph of lung section, revealing characteristic granulomatous interstitial reaction (× 150).

Case 2.—A 35-year-old man, also a farmer, was first seen as an outpatient on March 20, 1950. He reported that he had ceased smoking in November, 1949, because of a cough which was sudden in its onset. He had fever with temperatures as high as 102 F (38.8 C) and raised yellow sputum, which gradually increased in amount. Shortness of breath when he attempted to do any work was very troublesome. Recurrent episodes of fever, chills, and severe headache continued to occur about once a week. After four to five hours, he experienced a malodorous sweat. Between these episodes, he felt quite well. He had lost 25 lb. (11.3 kg.) since November, 1949. Fortunately, his wife, who accompanied him, was an observant individual. She volunteered the information that his periods of illness had always recurred when he felt well enough to return to doing his farm chores. The history was then obtained that, when he was working with moldy silage in 1946 or 1947, he had noted fever and headache after handling it but was not aware of any respiratory complaints. Before the illness in November, 1949, he had worked with moldy millet hay, and he had been working with the same material each time he had chills and fever. His brother, who had worked with the same moldy silage and hay, had suffered no ill-effects. Penicillin injections in February, 1950, had produced no benefit. The physical examination revealed fine crepitant rales at both bases. The blood cell count was normal. Agglutination tests for Brucella abortus were negative. Sputum cultures revealed Candida albicans. The chest roentgenogram showed the cardiac silhouette to be normal. There was a generalized loss in aeration in the lung fields, most pronounced at the lung bases. The diaphragms were smoothly rounded with clear sulci. A diagnosis of farmer's lung was made, and the patient was advised to avoid all contact with barn dusts.

In December, 1950, he was seen again. He reported that he had gained weight and that during the summer he had been well and had been able to do his regular farm work. In mid-October, 1950, his cough recurred and blood-streaked sputum was observed. Fever and night sweats were present. He had been working in the barn but had not been handling any moldy hay. On physical examination, numerous rales were present, especially at the right lung base. Chest x-ray on Dec. 15, 1950, showed clearing of the interstitial changes. There was a small homogeneous density at the right cardiohepatic angle. A distinct change in the cardiac silhouette was seen. There was a prominent convex bulge in the left midcardiac border. The allergy consultant found the patient to show slight reactions to tree and ragweed pollen and to stockhouse dust and barn dust. Desensitization with house and barn dust was recommended. On Feb. 12, 1951, a chest x-ray showed no clearing of the right lung changes. Cardiac fluoroscopy was done, and the prominence of the left cardiac border was believed to be explained by pleuropericardial adhesions. A bronchogram of the right lung was done because of the clinical suspicion of bronchiectasis, but the bronchial tree was found to be normal. Sputum cultures showed no fungi at this time.

In February, 1954, a note was received from a local sanatorium that the patient had been seen there because of extensive bilateral disease suggestive of tuberculosis but that tubercle bacilli could not be found on culture of sputum or gastric aspirate. In March, 1955, he was admitted to the Madison, Wis., Veterans Administration Hospital because of progressive difficulty. He was no longer able to work full time but had remained on the farm. He continued to cough and expectorate as much as one cup of sputum per day. The sputum had been blood-streaked on many occasions. There had been a weight loss of 22 lb. (10 kg.). Chest pain on the right side had been present during several of his more recent episodes of chills and fever. Increased shortness of breath had been a major factor in limiting his working ability.

On physical examination, he appeared to be acutely and chronically ill. Dyspnea occurred with the effort of sitting up. Numerous rales were heard, especially over the right lung. The heart was not enlarged. The pulmonic second sound was accentuated. The total blood cell count was normal. Numerous sputum studies showed no fungi or tubercle bacilli. Pleural thickening on the right side, obliterating the sulcus, and strands of fibrosis in the right upper lung field were the major changes seen in the chest roentgenogram (fig. 4). There were some granular nodules, chiefly in the lower lobes. The left lung revealed similar but less marked changes. On April 13, 1955, a bronchogram was done on the right side. There was considerable distortion of the bronchi and moderate cylindrical dilation of the medial basal segmental bronchi. A bronchoscopy was done April 12, 1955. The trachea was deviated to the right. Moderate redness and thick fibrinous exudate was observed in the right main stem bronchus. The lobar bronchi appeared normal. Cardiac catheterization revealed normal findings. On June 21, 1955, a surgical biopsy of the right lung was done (fig. 5). The pleural space was obliterated by adhesions. The lung specimen revealed a pleural thickening, fibrosis of the alveolar walls, and peribronchial fibrosis. No epithelioid or giant cells were found.

These two patients demonstrate very clearly the recurrent episodes of rather serious illness. Subsequent observation has shown, fortunately, that the younger man seems to be very little handicapped, since he has avoided continued exposure to the noxious materials. The second man originally had the same type of symptoms, but after continued exposures for eight years he reached the point of having marked permanent lung damage.

Comment

The diagnosis of farmer's lung requires an awareness of this illness. The evidence of the dust exposure, usually with moldy material, in the patient's history is not difficult to elicit. However, as such exposure is very common and frequently has been tolerated by the individual previously, he may not attach any significance to this. To complicate the problem further, many patients fail to recognize the possible correlation because their co-workers have suffered no ill-effects. Also, respiratory symptoms in the winter months and freedom from difficulty in the summer months may be interpreted as being due to recurrent respiratory infections. However, in this study a detailed occupational history usually demonstrated a close correlation between the exposure to dust and the onset of chills, fever, cough, headache, and shortness of breath within a few hours.

The differential diagnosis between this type of illness, usually termed farmer's or thresher's lung, and the more recently described silo-filler's disease[1] is not difficult to make in the usual patient. The latter illness is due to nitrogen dioxide irritation of the respiratory tract. These noxious fumes are created by the fermentation of nitrates in the forage placed in the silo. The period of production of these noxious gases fortunately is a transient one, usually starting within a few hours and not lasting more than 10 days to two weeks. There has been much attention directed to this hazard, so that most farmers are aware of the possible dangers. The gas is usually concentrated enough to be primarily irritant, so that the person has to leave the area promptly. Occasionally, a concentration may be present that is strong enough to cause immediate death. If the concentration is lower, the onset of symptoms may be delayed. The acute episode may be indistinguishable clinically and roentgenographically from farmer's lung. Autopsy and biopsy reports show acute edema in the fulminating cases and subacute bronchopneumonia with bronchiolitis fibrosa obliterans in the chronic cases. The latency between exposure to these gases and the development of the acute respiratory symptoms apparently depends on the concentration of the gases, as several patients have died within a few hours. In our experience, this is a much more uncommon illness than that seen secondary to contact with the moldy silage when the silo is opened for the first time and the large amount of mold is present. The history concerning the date of the silo filling, as well as the frequent recognition by the affected person that there was an unusual gas present, will clarify the diagnosis.

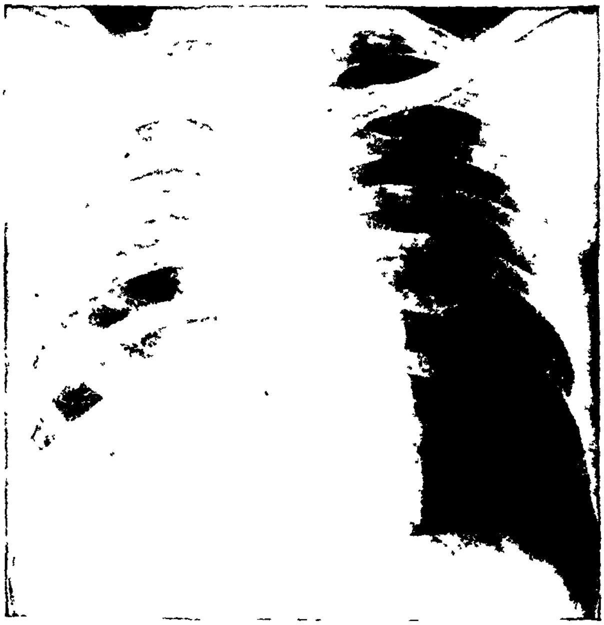
Fig. 4 (case 2).—Chest roentgenogram seven years from onset of illness. Marked pleural fibrosis is more evident than scattered stringy nodular densities in lung fields.

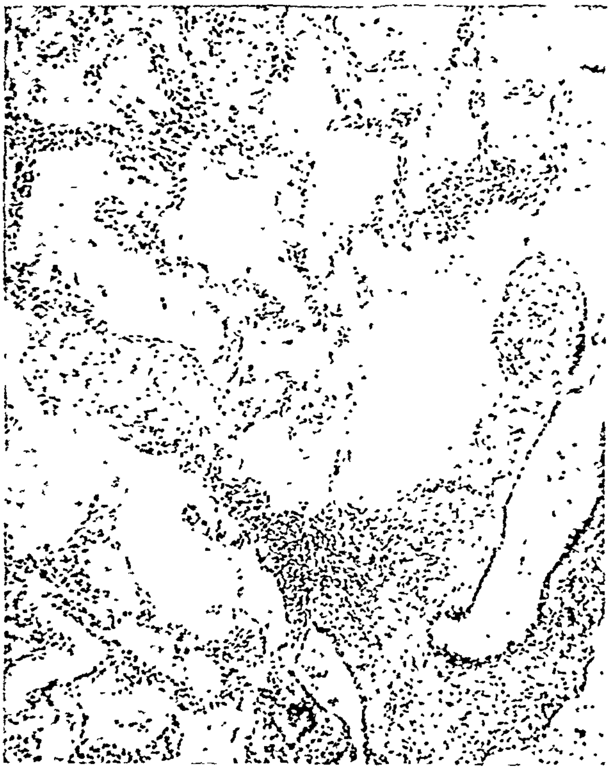
Fig. 5 (case 2).—Photomicrograph of lung section, showing alveolar walls moderately thickened and fibrous. No epithelioid or giant cells are seen (× 75).

The incidence of farmer's lung is a difficult problem to assess. However, we believe it to be much more common than a report of 39 patients would suggest. Many patients have minor episodes of this type of illness without recognition of the true nature of the illness. With the acute onset of chills, fever, and cough, supported by physical evidence of rales in the lung fields, pneumonia is a common diagnosis. Among older patients, the symptoms of dyspnea on exertion coupled with evidence of fine rales at both bases frequently lead to an erroneous diagnosis of cardiac failure. Repeated bouts of chills and fever without marked respiratory complaints suggest the possibility of brucellosis in a farmer. Bronchiectasis is frequently suspected. In several patients in this study, bronchograms were done because of this suspicion, but no bronchial abnormality was demonstrated except in the second bronchogram done on the patient in case 2.

On the whole, failure to establish the proper diagnosis during the initial acute illness will seldom impair the patient's chances of recovery from this episode, for most of these patients improve when they are removed from the offending dusts. The patient may, of course, have been subjected to unnecessarily prolonged hospitalization, costly laboratory investigations, and therapy with expensive antibiotics. Of more importance, however, is the fact that if the proper diagnosis is not made the farmer is likely to be reexposed to the offending agent. In some persons, this may produce alarming and potentially fatal acute pulmonary insufficiency. More commonly, continued reexposure results in a chronic inflammatory reaction in the lung or numerous subacute episodes of interstitial pneumonitis which ultimately produce permanent and totally incapacitating pulmonary insufficiency. The economic problems created by this illness are major ones, as the farmer usually has to leave the farm or hire help to do the work in dusty areas. As would be expected, there is a great reluctance on the part of these individuals to give up farming until they are forced to do so because of their inability to do the work. By this time, their pulmonary damage is usually so great that any manual labor, even in a dust-free environment, is not well tolerated. In our opinion, this disease would attract much more attention if it occurred in an industrial group where there is a greater concentration of individuals and where the problem of compensation might be raised.

Treatment of these patients has not been uniform, due in part to the wide variation in the clinical symptoms. The removal of the patient from further contact with the offending material is most important in the control of the symptoms. In the acutely ill patient, this is accomplished by his own illness. Unless there has been a very severe degree of pulmonary involvement, the patient frequently feels much better and the acute fever, as well as the cough, subsides after three to seven days. This fact has frequently led to the erroneous conclusion that the patient's "pneumonia" has responded to antibiotic therapy. However, the persistence of dyspnea on exertion is unlikely after bacterial pneumonia. In the acutely ill patient, steroids have been utilized with apparent benefit, although evaluation is difficult. In the patient who has persistent dyspnea and clinical evidence indicating residual interstitial pneumonitis, adrenal steroids have been utilized with marked subjective improvement in the disabling shortness of breath. The mode of action of adrenal steroids is undoubtedly complex, but suppression of tissue hypersensitivity, which we believe underlies the inflammatory phenomena, is a reasonable hypothesis. Also, adrenal steroids have been shown to be of value in other forms of pulmonary granulomatosis and in various diseases thought to result from tissue hypersensitivity. It appears logical to utilize them in an attempt to shorten the duration of disability and to lessen the residual damage. In our experience, iodides have been of little value.

The etiology of farmer's lung remains unsolved. In 1932, Campbell[2] presented a brief clinical report of a peculiar respiratory illness in five farmers seen in the months of April and May, 1932. The severity of their illness, which was associated with contact with "white mold" on hay and grain, prompted this excellent clinical description. He noted that the wet summer of 1931 had created an unusual amount of moldy grain and hay in Westmorland. Later, Fawcitt,[3] also of northwest England, published several articles on the same peculiar respiratory illness. He concluded that the disease was an actual mycotic infection of the bronchi.

In 1945, Duncan,[4] in a general discussion of fungus disease in Great Britain, commented on farmer's lung. He did not agree that this was a true mycotic infection. He questioned whether the mold in its growth on the hay produced some noxious substances or whether the mold, by breaking down the hay fibers, produced a sufficiently fine vegetable dust to cause, by inhalation, a disorder analogous to byssinosis of cotton-mill workers. He favored the latter concept.

Törnell,[5] in Sweden, reported on eight patients with the same type of illness who had been exposed to moldy grain in the threshing process. He used the term thresher's lung and concluded that these individuals actually had moniliasis of the bronchial tree.

Zettergren,[6] in 1950, reported on animal studies. Rabbits were exposed in a dust chamber for one hour for 10 successive days. Twenty rabbits (series A) were exposed to sterile threshing dusts, and 28 rabbits (series B_1 and B_2) were exposed to sterile threshing dusts mixed with viable Candida (Monilia) albicans. Series A and B_1 were sacrificed five days after the exposure was completed and those in Series B_2 10 weeks after exposure. Inhalation of sterile dusts caused submiliary histiocytic lung granulomas, which Zettergren labeled dust granulomas. With C. albicans added, submiliary-miliary tuberculoid granulomas (fungal granulomas) were found. The dust granulomas were of shorter duration than the fungal granulomas. The fungi did not multiply in the rabbit's lung.

Studdert,[7] in 1953, described four patients with farmer's lung. In his discussion, he expressed doubt as to the actual fungus infection and concluded that farmer's lung represented a nonspecific irritant, probably a foreign protein. In the same year, Fuller's review[8] of farmer's lung appeared. In eight years, he had collected 32 cases. He described three phases of the disease: "(1) the acute isolated attack, (2) the subacute and more chronic condition which shows a spontaneous tendency to recover, and (3) the chronic and irreversible phase where secondary lung changes such as emphysema and fibrosis have occurred as the result of repeated exposure over a period of years." He concluded that farmer's lung is the result of irritation of the bronchial epithelium by the breakdown of mold spores and possibly grass particles.

Soucheray,[9] in 1954, reported on three patients with farmer's lung. He suggested that farmer's lung was pulmonary moniliasis. In 1956, Williams and Mulhall[10] reported on 10 patients from Wales. They suggested that the respiratory difficulty is due to a plugging of the terminal parts of the bronchial system by the mold spores.

In addition to the reports of farmer's or thresher's lung, other reports of exposure to dust have appeared which seem comparable in clinical and roentgenographic descriptions. In 1932, Towey and co-workers[11] reported on 35 patients whose illness was believed due to the spores of a fungus tentatively identified as Coniosporium corticale, found in maple bark. Their concept of the pathogenesis of this illness is well stated in their summary: "It is our opinion that this illness is due to a local toxic effect and foreign body reaction combined with a delayed effort resembling protein sensitization in its clinical and certain immunologic aspects."

The illness reported by several authors[12] occurring among workers exposed to the sugar cane residual fiber, bagasse, is similar in clinical and roentgenographic pattern. Castleden and Hamilton-Paterson[12b] suggested that the acute phase was an allergic response. However, in the report of Sodeman and Pullen,[12c] the description of the needle biopsy of the lung in their patient and of the lung section from another patient who died with this disease is not that of an acute granulomatous interstitial pneumonitis. They reported an increase in the fibroblastic reaction of the interstitial cells. On examination with polarized light, small spicules were noted. In the needle biopsy specimen, a large piece of foreign material with the appearance of bagasse was noted.

In our opinion, farmer's lung is caused by the sensitization of the individual to the molds or the product of these molds. The causal relationship between the exposure to the moldy material and the illness seems evident. The exact role of the molds, dust, and individual susceptibility remains unknown. The onset of chills and fever within a few hours after exposure to the suspected noxious material is quite unlike the usual response to fungus infection of the lungs. The diffuse interstitial pneumonitis is not the pattern associated with some other fungus infections due to inhalation of the spores, namely, histoplasmosis and coccidioidomycosis. The clinical picture of chills, fever, and cough resembles much more closely that observed with the inhalation of tuberculoproteins in the individual who is sensitive to tuberculin. The microscopic changes in the lung are similar to changes noted in other conditions currently regarded as a tissue hypersensitivity response. Studies to clarify these factors are not simple because of the great complexity of the molds and the variation of the organic material, as well as the selection of a suitable experimental animal. The creation of a sensitivity prior to the "dusting" that might produce a pattern similar to the clinical disease is another problem.

At the present time, prevention of exposure seems to be the only logical course. It should be stressed to agricultural workers that these moldy materials are hazardous. If acute illness does not occur, it does not mean that the patient has not developed a sensitivity.

In Wisconsin, there is a greater chance for the development of farmer's lung than in many areas of the United States. The major farm activity is dairying. This requires the storage of a large amount of hay and grain for cattle feed. Climatic conditions which favor poor drying are common. The hay and grain are usually stored in poorly ventilated mows and bins. Once moldy hay has been in the mow, the area may remain contaminated for years, since the mows are rarely entirely emptied and cleared of the residual moldy material. Severe winters have resulted in the construction of relatively air-tight barns, which cause a higher and more prolonged dust concentration than would be present where feeding is done in the open lot or shed. In addition to these factors, silos are widely used for the production of corn and, more recently, grass silage. This material is frequently moldy on the top and edges when the silo is first opened. The dry, very dusty, moldy silage is tossed down the chute, and, frequently, the only source of air is from this chute. The dust concentration can be extreme.

Farmers must recognize the hazard and make every attempt to prevent the storage of wet material which will produce mold. The development and wider use of driers may be helpful in the control of this problem. If material has become moldy, then use of effective masks and even wetting down of the usually very dry and extremely dusty moldy material prior to handling must be considered. If the farmer realizes that the handling of moldy material may be a hazardous as well as a disagreeable task, farmer's lung may be seen less frequently.

Summary

Thirty-nine patients with farmer's lung were seen, and lung biopsy was done in eight patients. Six specimens revealed a granulomatous interstitial pneumonitis with epithelioid and giant cells.

Symptoms of shortness of breath, cough, fever, chills, weight loss, and hemoptysis occurring in individuals exposed to organic dusts should arouse the suspicion of farmer's lung. The roentgenographic evidence of an interstitial pneumonitis in patients with these complaints makes the diagnosis of farmer's lung almost certain. Farmer's lung is a potentially serious and crippling disease, believed possibly to result from a hypersensitivity response to molds or the products of molds occurring in a wide variety of organic material.

1300 University Ave. (6) (Dr. Rankin).

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A DISCOVERY OF THE FIRST MAGNITUDE.—I believe that the finding of Fraenkel-Conrat and Gierer and Schramm that virus activity may reside in a nucleic acid represents a discovery of the first magnitude, for it means that a polynucleotide of comprehendible structural complexity can carry the code of informational pattern not only for the production of more of the same polynucleotide but also for the de novo production of a highly specific polypeptide. It provides a much more sound experimental as well as theoretical base for contemplating the existence of the myriads of living things on earth. It is a discovery that is affecting the thinking and the course of events in virus research and all that virus research is concerned with, such as genetics, infectious disease, cancer and life itself. Eventually chemists should be able to synthesize a small polynucleotide specifically arranged, hence one may now dare to think of synthesizing in the biochemical laboratory a structure possessing genetic continuity and of all the tremendous implications of such an accomplishment. Studies of this nature and related studies could easily lead directly to the heart of the cancer problem and provide a solution to a situation which today appears so very perplexing.—W. M. Stanley, The Potential Significance of Nucleic Acids and Nucleoproteins of Specific Composition in Malignancy, *Texas Reports on Biology and Medicine,* Fall, 1957.

THE WESTERN RESERVE ANESTHESIA MACHINE, OXYGEN INHALATOR, AND RESUSCITATOR

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Anesthesia can be induced quickly and maintained for periods of 3 to 20 minutes in obstetric, pediatric, dental, and traumatic cases by administering cyclopropane with helium and oxygen from thumb-sized cylinders. The mixture of 30% oxygen, 30% helium, and 40% cyclopropane is nonexplosive. Administration is accomplished by an easily portable machine here described. This midget type of anesthesia machine has been used to anesthetize more than 8,500 patients in the course of five years. It has also been uses successfully in asministering oxygen in units of 3,400 cc. for resuscitation or for brief periods of oxygen therapy. Because of its simplicity the machine is easily refilled or disassembled for cleaning. Clinical experience and laboratory data have shown it to be safe and effective when properly used.

Since 1933 cyclopropane as an anesthetic, introduced by Ralph Waters at Madison, Wis., has assumed an ever-increasing place in anesthesiology. The fact that this agent is flammable has limited its use in many small hospitals, operating rooms, and physicians' offices, where conditions did not permit costly explosion prevention.

In March, 1953, members of our Western Reserve University department of anesthesia, department of chemistry, research medical students in the new educational phase program, a professor of physics of Case Institute, and the engineering department of a Cleveland manufacturing company combined forces and efforts to package an instantaneous nonexplosive anesthetic mixture containing 30% oxygen, 30% helium, and 40% cyclopropane, or 100% oxygen if required for inhalation or resuscitation.[1] These mixtures are packaged in thumb-sized cylinders, especially adapted for a small, 2-lb. aluminum anesthesia machine,[2] which can serve also as an oxygen inhalator and resuscitator (fig. 1).

Use as an Anesthesia Machine

A wide variety of pediatric, obstetric, and surgical operations have been performed with use of the anesthesia machine, without serious complications. The most frequent uses are listed below. 1. For children, prompt, pleasant induction into plane 2 anesthesia with 4 to 20 breaths prior to developing maintenance anesthesia with open drop ether for tonsillectomy and adenoidectomy (4,481 cases) (fig. 2). 2 Obstetric anesthesia for delivery of normal multiparas, for periods of 3 to 12 minutes (394 cases).[3] Episiotomy was done or lacerations were repaired under local anesthesia supplement, as patients emerged from sleep two to five minutes after removal of the mask. In a small percentage it was used for forceps application and in rapid delivery in complicated cases requiring instantaneous delivery because of fetal distress. As an example, forceps deliveries have been effected after 12 to 14 breaths of the mixture. In two instances version and extraction for prolapsed cord were completed three minutes after start of anesthesia. 3. As a supplement to thiopental (Pentothal) sodium for dilatation and curettage in more than 100 cases. 4. In dental surgery for multiple extractions of 2 to 20 teeth in 526 cases.[4] Anesthesia developed to plane 2 surgical stage following 8 to 50 breaths, which correlated with blood stream levels of 9 to 16 mg. of cyclopropane for each 100 cc. of arterial blood. 5. In pediatric orthopedic manipulations of deformities of extremities and in greenstick fractures, 250 cases. 6. With and without muscle relaxants and/or sleep doses of thiopental for intubation, 190 cases. 7. In short five-minute operations such as single and bilateral myringotomy, suture of lacerations, and incision of abscesses or removal of abdominal and perineal packs, 85 cases

Nonflammable Mixtures of Cyclopropane.—In June, 1954, E. C. Gregg,[5] the professor of physics of Case Institute in Cleveland, considered the relative hazards of explosion associated with the Western Reserve portable anesthetic machine with anesthetic mixtures of cyclopropane and oxygen. as compared to the presently used standard equipment with the same calculated mixtures of the gases. He stated in a personal communication to me:

> The hand unit possesses not more than about one-third of the destructive potential of a standard machine from the viewpoint of primary electrostatic explosion This ratio becomes very much smaller if one considers an explosion of a standard machine with a leak or an open port such that most of its bottled cyclopropane escaped to the atmosphere and there formed an explosive mixture in the operating room For a secondary explosion of this kind, assuming a bottle of 378 liters capacity and a room with no ventilation, one

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Read before the Section on Anesthesiology at the 106th Annual Meeting of the American Medical Association, New York, June 6, 1957 would obtain a minimum lower figure of 1 to 240. One could go still further and estimate tertiary effects of knocking over larger bottles of gas in the room and igniting these; however, the major danger here would be from fire rather than explosion, since there would be a slow formation of an explosive mixture. Under any circumstances the portable unit appears very much safer than a standard gas machine.

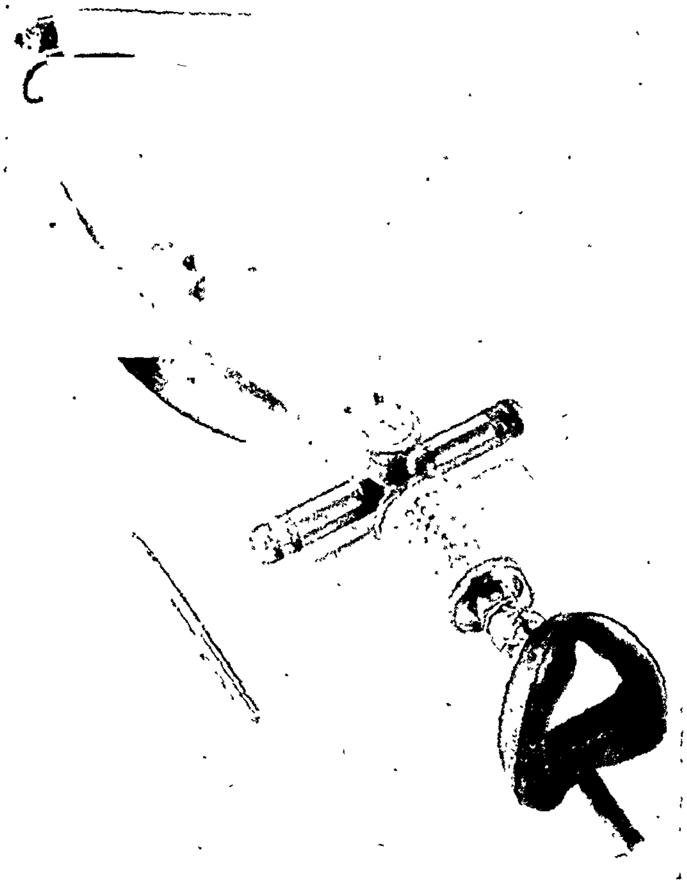

Fig. 1.—The Western Reserve Miniature Anesthesia Machine and Oxygen Resuscitator.

Nevertheless, the use of cyclopropane, ethylene, ether, vinyl ether, ethyl chloride, and most of the recently developed ethers for anesthesia has resulted in potentially explosive mixtures that have in the past been associated too frequently with electrostatic ignition leading to death or serious injury of the patient and with other disasters.

Therefore, in May, 1954, we began to consider means of developing a packaged nonexplosive anesthetic mixture. With C. A. Brown,[6] associate professor of chemistry at Western Reserve University, we reviewed all of the nonflammable mixtures of anesthetic gases developed and the possible additives for cyclopropane-oxygen mixtures. Using the recommendations of Jones and his co-workers [7] and Hickcox [8] concerning the per cent by volume composition of nonexplosive anesthetic mixtures (see table), we have developed nonexplosive mixtures of cyclopropane, oxygen, and helium or nitrogen. We verified the nonexplosibility of our mixtures by placing them in an explosion chamber (fig. 3), and tested for flammability by means of electric spark and flame ignition. The fact that no explosions occurred in our tests with these mixtures confirmed previously published data.

These mixtures have been tested in more than 8,000 short anesthesias in order to determine the safest and most effective mixtures that would preserve the highest concentrations of oxygen, the most rapid induction of anesthesia, and the minimum of undesirable side-effects. To assist us in our determinations of the efficiency of the anesthetic and of safety to the patient, we have in many instances carried out the following studies before and during induction and maintenance of various depths of anesthesia in both children and adults undergoing surgical, obstetric, and dental procedures: electrocardiographic and electroencephalographic studies; spirometry determinations; blood pressure, pulse, and cardiac output measurements; and determination of blood levels of cyclopropane, oxygen, and carbon dioxide. We found that there was no undue depression of vital physiological function below plane 2 of anesthesia in any case.

Having determined what were to be the components of the mixtures, in consultation with George J. Thomas and the testing laboratory of the United States Bureau of Mines, we began the packaging in thumb-sized cylinders of compressed mixtures of cyclopropane and helium and of oxygen and helium in the proportions of nonexplosive potential as defined in the table. Combination of the contents of one cylinder of each type in the machine gives an anesthetic mixture that is nonexplosive. The cylinders are painted different colors for easy rec-

Fig. 2.—Three-liter duck decoy rubber toy bag for inductions of anesthesia in babies and small children.

ognition, and a green cylinder containing the compressed equivalent of 3,400 cc. of oxygen at atmospheric pressure is available for resuscitation and inhalation.

Since the optimal conditions for explosion exist when there are eight parts of oxygen to two parts of cyclopropane, it is obvious that the higher the concentration of cyclopropane, the safer the mixture. This fact has been confirmed by our tests for explosibility of mixtures of cyclopropane, oxygen, and helium in varying proportions. Furthermore, our clinical studies revealed that induction of anesthesia is effected more promptly and smoothly with higher concentrations of cyclopropane. Through a series of clinical tests, we have determined the mixture that produces the most satisfactory clinical results: The green and brown cylinder contains 1,850 cc. of oxygen and 470 cc. of helium; the orange and brown cylinder contains 2,200 cc. of cyclopropane and 1,180 cc. of helium (with recessed metal cap as safety pin index). These cylinders yield 6,000 cc. (30% oxygen, 30% helium, 40% cyclopropane). If the components of this mixture are packaged in two thumb-sized cylinders, with sufficient oxygen and helium in one cylinder and sufficient cyclopropane and helium in the second cylinder to make 6 liters of gas at atmospheric pressure, the mixture remains nonexplosive during the induction of anesthesia in patients of all ages, provided that no pure oxygen is added to the mixture faster than it is taken up by the blood stream.

Per Cent by Volume Composition of Nonexplosive Anesthetic Mixtures of Cyclopropane, Oxygen, and Helium

Cyclopropane	Oxygen	Helium
15	20	65
20	20	60
25	25	50
30	30	40
40	30	30

Safety-Pin Index System.—The perforating pin on the orange-designated side is twice the length and size of that on the green oxygen side, and fits exclusively into the recessed metal convex cap of the anesthetic cylinder; while the perforating pin on the oxygen and helium or oxygen side designated by the green band is of smaller size and perforates exclusively the unrecessed metal cap of the oxygen and helium or oxygen cylinders. This safety device eliminates the possibility of the simultaneous use of two anesthetic cylinders to the exclusion of oxygen in the proportion well above the 20% found at atmospheric pressure.

Laboratory Correlation of Clinical Results.—In this phase of our study we have used the 40% cyclopropane–30% oxygen–30% helium mixture in the anesthetization of 79 test patients of varying ages, weights, and physical conditions undergoing surgical, obstetric, and dental procedures. During these anesthetizations 529 samples were taken from the rebreathing bag of the machine into 20-cc. vacuum tubes, as illustrated in figure 3, and more than 2,000 quantitative and qualitative gas measurements were done by the chemical method described by us in a previous publication. Cyclopropane was absorbed from the mixture in the Haldane-Boothby-Sandiford apparatus (modified by us) by means of sulfuric acid. Carbon dioxide was absorbed from the residue mixture by potassium hydroxide. Oxygen was absorbed from the final residue mixture by potassium pyrogallate. After cyclopropane, water vapor, carbon dioxide, and oxygen were absorbed from the samples in the rebreathing bag, the final residue could be considered to be nitrogen and helium—both inert diluents and nonexplosive buffers.

Statistically useful data are available for 6 minutes of anesthesia for all of these cases; recently we have determined additional information in other cases from 12 to 90 minutes of such administered anesthesia. In these 79 patients, plane 1 or 2 anesthesia was induced after 6 to 12 respirations without exception. At all times during the first six minutes of anesthesia the proportion of oxygen in the mixture in the closed system remained above 20%, and the cyclopropane level gradually diminished from 40 to 20%. Initial oxygen concentrations averaged 29% at the beginning of the anesthetization and 23% at the end, while the level of cyclopropane

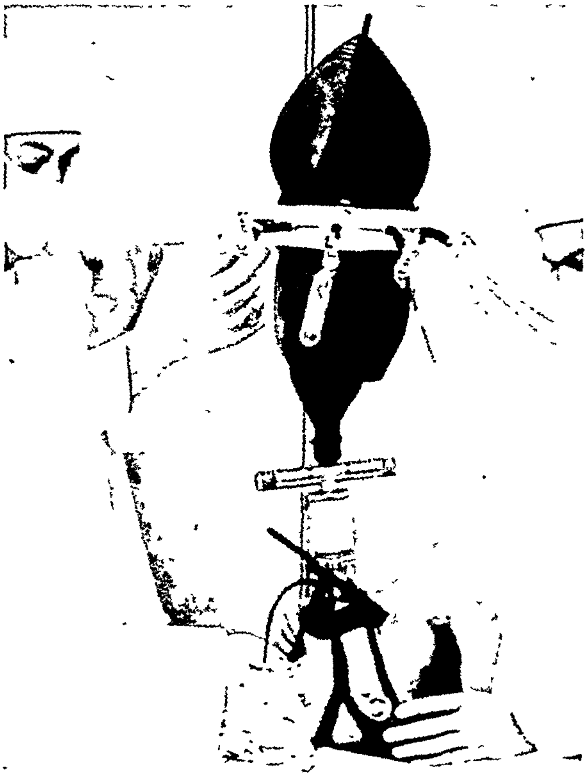

Fig. 3.—The Western Reserve Midget Anesthesia Machine with special circumferential ports with 10 20-cc. sampling vacuum tubes for qualitative and quantitative gas analysis.

in all cases had fallen into the safety range below 25% after six minutes. When a 100-cc. soda lime canister was used with fresh material, the carbon dioxide content of the rebreathing bag remained below 3% after six minutes.

Ninety-six per cent of the samples were outside the spark and flame ignition range; 3% revealed that the mixture had momentarily moved into the flame ignition range; and 1% of the tests revealed a momentary spark ignition range. However, a substantial number of these flammable samples were predictable because pure oxygen had been added to the anesthetic mixture. In the light of our recent experience, a further number could have been made nonflammable through our presently used precaution of weighing the filled cylinders on a microscale. The underfilled cylinders representing by weight an error of plus or minus 3% are discarded. The approximately 1% of unpredictably potentially dangerous samples were probably due to mechanical failure. Already progress has been made in eliminating this hazard entirely.

When one considers that an anesthetic explosion presently occurs no more frequently than 1 in 75,000 with presently used safeguards, the reduction of anesthetic explosion potential by at least another hundredfold represents a substantial progress in permitting the return of safer and more predictable *instantaneous anesthesia* to the emergency outpatient room, the properly equipped dental office, the accident admitting division, the x-ray room, and, of greater importance, the military bases and warships at sea presently denied this essential service.

Use as an Inhalator

The first objective in the design of the equipment has been the adaptation of portable, readily accessible oxygen for resuscitation and for use in a therapeutic closed inhaler and escape gas mask. This has been accomplished by engineering design of a compact 2-lb. unit easy to operate and efficient in its provision of oxygen in atmosphere, stabilizing after several inhalations at 60% to 80%; of equal importance is its absorption of carbon dioxide with a closed to and fro canister system offering the minimum of resistance. The latter has been accomplished for as long as necessary with canisters of 100 cc. for 15 minutes, 200 cc. for 30 minutes, or 350 cc. for up to two hours.

The oxygen is packaged under pressure of 4,000 lb. per square inch in 10-cc. metallic containers about the size of the thumb, capable of holding about one free volume gallon (3,400 cc.) or sufficient oxygen for an adult at rest for 10 minutes per cylinder or the oxygen requirements when walking at a rate of 3 miles per hour for 200 yd. By a simple wrist turn of the side-arm container of the cylinder, the compressed gas is readily released through directional ports into a 6½-liter rebreathing bag by a perforating pin mechanism.

Method of Operation.—Press the mask firmly on face, with special attention to leak-proof fitting around bridge of nose. A red band will be noted around the snap assembly unit just above the mask. When the mask is pressed firmly to the face, the release valve will open. The red band will then disappear, indicating an unobstructed oxygen flow into the mask.

Use as a Resuscitator

Oxygen in the Physician's Satchel.—Neither the 10 phamaceuticals in the physician's satchel of a quarter century ago nor the 10 wonder drugs in his satchel in 1957 contain the most essential element for saving life, namely, oxygen. Yet, promptly and properly administered by general practitioners, pediatricians, dentists, or by members of the surgical specialties, 100% oxygen in the alveolar reservoirs (lungs) is the agent most needed and most effective in maintaining life.

Hypoxia is usually the precursor of death in disease, fatal accidents, under anesthesia, in infant resuscitation, and in fire and military disasters, yet a very small percentage of physicians, nurses, or rescue personnel could initiate or maintain a clear airway in the unconscious obstructed patient. Fewer still could develop the optimal respiratory cycle through artificial respiration effecting an adequate tidal volume or proper positive atmospheric and negative pressures to deliver oxygen and eliminate carbon dioxide.[9]

In emergencies associated with hypoxia the modern physician relies too greatly upon pharmacological injections. This is particularly serious when the needed treatment is oxygen, an unobstructed airway, elimination of carbon dioxide, and a return of blood to the heart sufficient to yield the next essential beat. *The use of autotransfusion* by elevating the legs will supply the central circulation in a few seconds with 600 cc. of well-matched blood which can be maintained by such devices as ace bandages or elastic stockings.

Paluel Flagg, in the August, 1953, issue of *General Practitioner*, strongly stated the obligation of the physician to reduce the death toll and brain damage due to lack of oxygen, which he stated to be twice that due to automobile accidents. While millions are being spent annually to reduce the automobile accident death rate, why is the situation in relation to oxygen lack allowed to remain the same? There are two basic reasons:

1. Lack of proper education for both physician and lay rescue squads in recognizing the need for and in performing resuscitation. Even when the necessity is recognized, the limitations of the generally used manual method of artificial respiration are not fully understood. As the need for resuscitation increases, often less than 150 cc. of air can be forced into the lungs by this method. This roughly corresponds to the dead space in the respiratory system, which does not come in contact with the alveolar membranes through which oxygen passes into the blood stream.

2. Lack of proper resuscitation apparatus that is convenient for use by all types of rescue personnel. The apparatus should be (*a*) readily available and easy to operate; (*b*) easily portable so that patients do not have to be moved before assistance is given; (*c*) safe in operation, i. e., designed to prevent any damage to the patient during resuscitation even by inexperienced laymen; (*d*) simple to operate, necessitating only limited training with the equipment.

Attempts at proper education are constantly being made by medical schools, civil defense units, police and fire departments, Red Cross units, and other groups interested in this problem. Emphasis is placed on immediate treatment to free the patient's airway of obstruction and to get oxygen to the lungs as soon as possible to prevent irreversible brain damage. Various methods are usually presented, from the simplest to the use of complex machines. If the patient receives adequate oxygen therapy before his circulation fails, it does not matter how it is given. Probably the most effective simple method is the use of the Safar double airway.

The Western Reserve University device meets these requirements. This machine can provide oxygen conveniently, both as inhalator and as resuscitator, under many conditions: 1. For the general practitioner. This device will readily fit into his bag. 2. For the rescue squad. It can fit into a man's pocket. 3. For the home cardiac, asthmatic, or anemic patient in temporary distress. It is instantaneously available at the bedside.

Technique for Use as a Resuscitator.—When this device is to be used as a resuscitator, it is important that the patient be lying on his back with feet higher than his head, in order to (1) initiate greater blood return to heart to aid maintenance of blood pressure; (2) help clear the lungs and bronchi of any foreign matter. Special attention should be given to clearing the throat of any obstruction before the unit is applied to the patient. This may be accomplished under direct vision, by use of suction apparatus or mouth suction through rubber tube or soda straws. An unobstructed airway to the lungs is essential and can be insured by means of the Guedel airway (rubber or plastic) of proper size (adult, child, or infant) (fig. 4). If not available, lift the lower jaw forward and upward by extending head on neck, supporting the angles of the jaw. Hold chin up. In cases of drowning a suction is useful, but oxygen under intermittent pressure should have priority. After a clear airway is established, the machine is placed on victim's face, with mask fitting snugly, and headstrap is snugly applied. With the last two fingers of the left hand of operator the patient's jaw is supported. The thumb, index, and middle fingers keep pressure on face mask. The right hand compresses and releases bag rhythmically 12 to 15 times per minute, with sufficient pressure to force oxygen into victim's lungs. The amount of pressure necessary can be determined by observing chest expansion and deflation during respiratory cycle. It is not necessary to press the bag too firmly. There is a pressure-limiting safety valve, set at +20 mm. Hg to prevent overinflation of the patient's lungs.

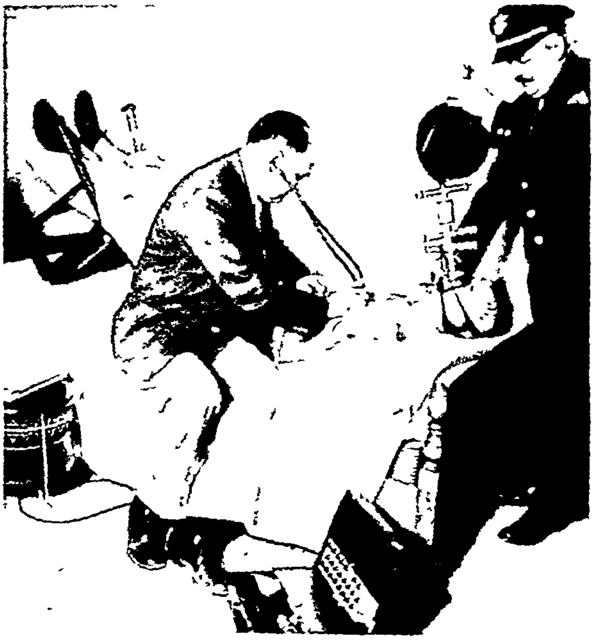

Fig. 4.—Proper application of specially equipped Western Reserve Resuscitator to patient's face in respiratory arrest. Note this machine is equipped with two additional central axial bodies, maintaining a combined loaded capacity of 6 oxygen cylinders or 20 free volume liters of 100% oxygen. If leaks are avoided this is sufficient oxygen for more than 30 minutes of resuscitation.

The operator should make sure the bag is inflated at all times, i. e., as soon as the bag is half empty, add another cylinder. This enables the operator to exert more efficient positive pressure on the bag, as well as keeping down the carbon dioxide volume percentage. Removal of the machine should occur only when the victim shows signs of recovery.

If the machine is equipped with the 100-cc. canister of soda lime, it may be used for approximately 20 minutes without a dangerous amount of carbon dioxide building up. However, if fresh soda lime is not then available, the machine should be removed from the victim's face and the bag should be emptied completely and refilled with pure oxygen; this procedure should be repeated each five minutes.

The physician may recommend this machine to his patients for self-administration as an inhalator, following the same rules of safe oxygen therapy as previously outlined.

Care of Western Reserve Machine

Of special significance in tuberculosis and respiratory infection, the Western Reserve machine may be disassembled completely and washed in lukewarm soapy water, with use of a toothbrush to scrub the metal parts. All parts should be rinsed thoroughly and the bag hung up to dry with loop provided. It is recommended that this be done periodically, to prolong the life of the unit. After repeated use of the Western Reserve unit the soda lime will turn whitish in color. The soda lime must then be changed and reactivated by removing the canister and refilling with a fresh package of soda lime; care should be taken to blow out dust. (The used soda lime may also be activated by placing it in a dish and putting it in a 250 F oven for 10 to 15 minutes, or until the lime turns to its natural color —pink.)

Carbon Dioxide Studies

Our carbon dioxide studies have revealed that the use of a 200-cc. soda lime canister provides a removal of carbon dioxide for periods of one hour in adults. Carbon dioxide is kept below 3 vol. % in this closed ventilation system of artificial respiration. Therefore, this canister should always be used for periods longer than 5 minutes, whether the equipment is being used as an inhalator, resuscitator, or anesthesia machine.

At the time of writing, the machine has been tested thoroughly for a period of three years with a research staff of six medical students, three university professors of physics, chemistry, and anesthesia, and three design engineers; its use can be documented in more than 8,000 short anesthetic procedures and operations in our hospitals and more than 2,000 additional cases from physician research consultants in other universities and hospitals in the United States, Canada, Great Britain, Europe, South America, and Japan. This machine has been used successfully in 2 cases in which it was the sole source of oxygen in treatment of cardiac standstill and in an additional 28 reported cases of serious respiratory arrest during anesthesia or as a result of traffic accidents.

Summary and Conclusions

During the past five years a new midget portable model anesthesia machine, oxygen inhalator, and resuscitator has been developed. To date more than 10,000 patients have been anesthetized with this machine, which utilizes nonexplosive mixtures of cyclopropane, helium, and oxygen, without major complications in the previously designated categories. In two cases patients with diagnosed cardiac standstill have been restored with the sole source of the oxygen used in the resuscitation coming from the thumb-sized cylinders. Babies and children responded favorably psychologically to the toy-sized and colorfully attractive machine and went promptly to sleep without struggling or excitement after the 4th to 12th breath. We have also had good results in obstetric patients with accelerated terminal labor, ambulatory dental patients, and patients requiring emergency anesthesia.

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OXYGEN THERAPY—AN UNSUSPECTED SOURCE OF HOSPITAL INFECTIONS?

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A humidifying device typical of the apparatus generally used in connection with oxygen therapy was studied bacteriologically as a possible source of contaminant organisms in the hospital. Samples of water taken from the reservoirs of the humidifier revealed a marked degree of contamination in a large percentage of cases. Although most of the bacteria found were nonpathogenic, a few were dangerous, and the extent of contamination was greater than had been anticipated. As a result, a systematic procedure for the care of humidying units in oxygen therapy has been adopted. The water to be used must be sterile, and when the level in the reservoir falls- the residue must be discarded and replaced, not merely replenished. Certain policies regarding sterilization should be followed, and after each period of use the glass reservoir must be cleaned and inspected before the unit is used again or stored.

Oxygen, as an essential part of modern therapy, has been extensively investigated, but bacteriological study of the apparatus used in this form of therapy seems to have been neglected. A review of the available literature on oxygen therapy in general and on humidification apparatus in particular has failed to provide any information on this aspect other than general statements, such as "The entire unit can be dismantled and sterilized in an autoclave."[1] Even where such statements are made, no reason is given for this use of the autoclave, other than the general, obvious, and unspoken one that all therapeutic apparatus should be clean.

This investigation was accordingly undertaken to determine three things: 1. In the efficient, well-run oxygen therapy unit of a modern teaching hospital, is contamination of the apparatus a real factor or only an imaginary hazard? 2. If contamination does exist, does it involve pathogenic organisms or only harmless saprophytes? 3. If contamination by pathogenic organisms is a real hazard, what modifications in procedure would be necessary to ensure sterile, or near sterile, operation?

Materials and Methods

Since no investigations had been reported, it was necessary to improvise and test methods of sampling, as well as to decide which pieces of apparatus, and how many parts of each piece, required investigation.

The figure shows a humidifier (Oxifier) of the type which comprised about 85% of the humidifying apparatus in the hospital at the time this investigation was begun. The several other types of apparatus in use need not be considered further, since they presented similar problems in sampling and the findings were essentially the same as those reported for this type.

The attachment and pressure-release valves (figure, *A* and *B*) were sampled with a swab moistened in sterile saline solution. Tubes of thioglycollate glucose broth were then inoculated and incubated at 37 C for four days. The water reservoirs were tested by removing 5 ml. of water with a sterile pipet. This was then either cultured in a flask containing thioglycollate glucose broth or else used for plate counts.

The oxygen coming into and leaving the humidifier and the outlet ducts in the humidifier could not be tested by these techniques. The system devised was based on the use of sterile tubing to bubble oxygen through a culture medium. Standard Bunsen tubing was cut into 10-in. lengths, placed in individual paper wrappers which were stapled shut, and put into an autoclave at 15 lb. of pressure for 20 minutes. This ensured a supply of sterile tubing which was easy to prepare and store. The medium used throughout was thioglycollate glucose broth. Fifty-milliliter amounts were placed in 6-oz., round, screw-capped bottles and put into the autoclave. When the incoming oxygen was being tested, the sterile tubing was attached to the connection at the upper end of the flowmeter (figure, *C*). The other end of the sterile tubing was placed just below the surface of the medium in the bottle and the oxygen run at exactly 5 liters per minute for exactly four minutes, thus ensuring each time that a comparable sample of 20 liters of oxygen was tested. There was no constant or reproducible difference in results, whether the oxygen ran at 2, 4, 5, or 6.6 liters per minute. However, the slower rates made sampling very tedious, and faster rates resulted in rather excessive splashing, so that 5 liters for four minutes was chosen as the best compromise and adhered to throughout.

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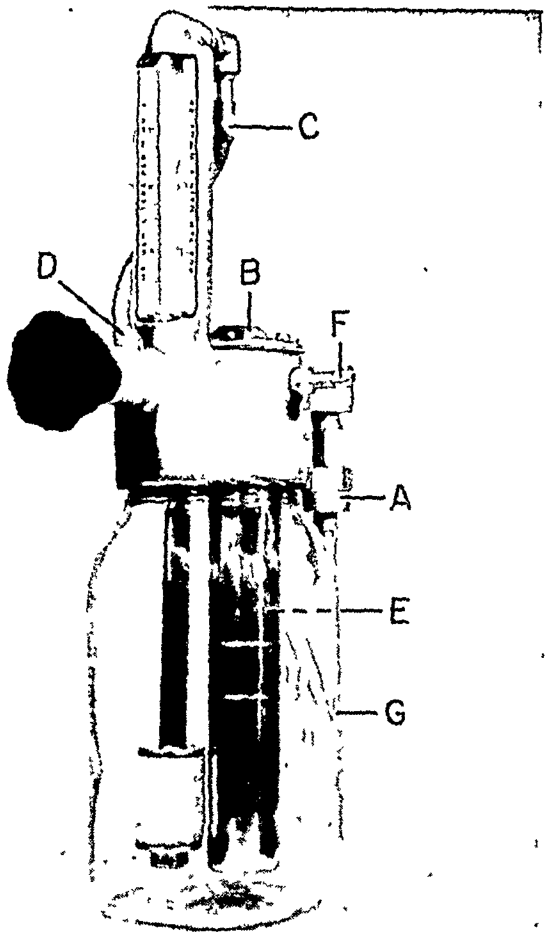
To sample the condition of the outlet ducts in the humidifier, without interference from organisms carried over from the water reservoir, duplicate reservoirs were filled with water to the usual level, paper covers were attached, and the reservoirs then put into the autoclave. These sterile reservoirs then replaced the regular reservoir, sterile tubing was substituted for the outlet connection, and the sample was taken as described above.

The patient delivery tubing was in 6-to-9-ft. lengths. It was sampled before and after cleaning by running 10 ml. of the sterile thioglycollate medium into one end, with the other end pinched closed. With both ends pinched closed, the broth was run from one end to the other several times by elevating alternate ends and was then decanted into a sterile test tube for incubation at 37 C for four days.



Humidifying apparatus in general use at time of investigation: *A*, attachment to wall outlet; *B*, pressure-release valve; *C*, flowmeter outlet tubing, upper end, *D*, flowmeter outlet tubing, lower end; *E*, tube to outlet with baffle-plate at top; *F*, patient outlet; *G*, glass reservoir.

Results

Testing of the oxygen from the upper flowmeter outlet and from the wall-connection itself showed uniformly sterile cultures, with the exception of an occasional organism which was almost certainly the result of accidental contamination, since completely aseptic sampling technique is virtually impossible. Swabbing of the pressure-release valve gave equally negative results.

As shown in table 1, the samples of water taken from the reservoirs revealed a marked degree of contamination in a large percentage of cases. The degree of contamination of the outlet ducts was also high, though not so marked as that of the reservoir water, and there was a lack of correlation in the number of organisms recovered from the two sources in individual pieces of apparatus.

The water used in the reservoir bottles was distilled, though not sterile, and it was difficult to understand why there was such a variation in the number of organisms present as well as such a high general level. Further investigation showed that there were four sources of contamination of this water: (1) the carboys in which the water was delivered to the hospital, (2) the siphon (rubber and glass tubing) used to withdraw water from these carboys, (3) the bottle used to take water around to the rooms in order to replenish the reservoirs of the units in operation, and (4) the habit of replenishing the reservoir bottles periodically as long as the unit was in operation for the same patient without first emptying out the remaining water.

It was found that there was no regular, automatic cleaning of the carboys at the source of the distilled water supply. As a result, distilled water only a day old was found in some cases to have a count of over 2,000 organisms per milliliter. A simultaneous check of a commercial distilled water advertised as being in "sterilized containers" showed that six carboys had a count of from 3 to 1,500 organisms per milliliter.

Contamination of the water was easily eliminated by switching to the use of commercial, sterile, distilled water. Cleaning the outlet ducts of the humidifiers (figure, *E* and *F*) was more of a problem. Several methods were tried. Originally, the ducts were rinsed through with disinfectant, followed by detergent and then by tap water. Next, the detergent was used before the disinfectant, followed by tap water and distilled water rinses. Another method employed was to hook the unit over the edge of a container full of a cationic detergent in such a way that the outlet ducts were below the surface while the release valve and the flowmeter remained dry. The unit was allowed to soak overnight and was then thoroughly rinsed. Finally, when these methods had been proved to be unsatisfactory, the unit was disassembled as far as possible and cleaned with a swab soaked in detergent, rinsed, and reassembled.

All these procedures failed to ensure even a reasonable degree of cleanliness (table 1), although the percentage of grossly contaminated reservoirs was considerably reduced. It was obvious that use of the autoclave would be the method of choice, but it was hoped to avoid this, since both the pressure-release valve and the flowmeter would be damaged. However, a later model of the same humidifier, the Oxijet, is made from stainless steel, including the release valve, and appears to be suitable for autoclave sterilization.

With regard to the types of organism recovered from the humidifying apparatus in this survey (table 2), it will be noticed that the majority are Enterobacteriaceae of a type falling under the general designation of "water bacilli," that is, of a type commonly recovered from water supplies and usually nonpathogenic for man However, a variety of organisms was found, possibly the most alarming of which was a gas-producing Clostridium, finally classified as an atypical Cl. perfringens (Cl. welchii). Fortunately, the apparatus from which this was isolated was not in use. It was on a surgery floor, but there is no record that any patient in that room suffered from gas gangrene. The outlet tubings were, in general, clean, only light growth of Staphylococcus pyogenes var. albus or of diphtheroids being recovered from the washings.

TABLE 1.—*Cultures of Humidifier Reservoirs and Outlets*

	Reservoirs							Outlets						
		Contamination							Contamination					
		Gross*		Slight†		Total			Gross		Slight		Total	
	No of Samples	No	%	No	%	No	%	No of Samples	No	%	No	%	No	%
Original sampling	46	27	59	14	30	41	89	37	5	14	12	32	17	46
Sampling after revision of cleaning technique	15	3	20	10	67	13	87	15	2	13	10	67	12	75

* Gross contamination determined by visible growth in less than 18 hours
† Slight contamination determined by visible growth in more than 18 hours

Comment

The results obtained were unexpected. Since the equipment was not routinely sterilized, some contamination was inevitable, but the extent was greater than had been anticipated. Secondly, the oxygen therapy service, to an impartial observer, appeared to compare very favorably with similar services encountered in other hospitals, as regards organization, cleanliness, and concern to improve methods and service. This inevitably raises the question as to what would be found on similar investigation in other establishments. It appears unlikely that conditions are much better elsewhere, from discussions held with people directly concerned with such matters.

With regard to the third question asked at the beginning of this article, before attempting to provide an improved service one must bear in mind several factors. In the first place, the difficulty of obtaining suitably trained personnel being what it is, the system should be as simple and reproducible as possible, to avoid undue expenditure of time by highly trained personnel. Secondly, it should not be prohibitively expensive. Thirdly, a careful balance needs to be struck between what is practicable and what is actually required. For example, aseptic technique throughout would not only be prohibitive in terms of both time and money, but it would be quite unjustifiable, since the air of the room itself is always heavily contaminated. However, it is justifiable to aim at a high degree of cleanliness, since the organisms present in the stream of oxygen are being introduced, under conditions favorable for the establishment of infection, into patients whose pulmonary mechanics render them particularly susceptible to infection. Although no accurate figures exist as to the frequency of patient infection resulting from contaminated oxygen therapy apparatus, it was unanimously agreed by all concerned that this final proof was not necessary. The weight of circumstantial evidence was considered sufficient to justify an immediate change in technique.

For these reasons, the following points were adopted in the Ohio State University Health Center: 1. All water used in humidifying apparatus must be sterile. 2. No apparatus can be in service for a patient for longer than one week. 3. The water in the humidifier must be discarded and replaced when the level falls due to use. The humidifier cannot be replenished without first emptying it. 4. Each time service is discontinued, or after a period of one week of service, the glass reservoir

TABLE 2.—*Analysis of Organisms Recovered from Reservoirs and Outlets of Humidifier*

Type of Organism	Times Found No.*	% of Total No of Samples
Achromobacter and Alcaligines fæcalis	33	29
Pigment producing bacilli (various types)	14	12.5
Staphylococcus pyogenes var. aureus (coagulase positive)	12	10.5
Diptheroids	3	2.7
Clostridium perfringens (Cl welchii)	1	0.9
Bacillus subtilis	3	2.7
Staphylococcus pyogenes var. albus	4	3.5
Pseudomonas aeruginosa	6	5.3
Yeasts and fungi (nonpathogenic)	3	2.7
Streptococcus viridans	1	0.9
Enterococci	1	0.9
Paracolon bacilli	1	0.9
Escherichia	1	0.9
Klebsiella	1	0.9
Nonpathogenic mycobacterium	2	1.8
Sterile samples	29	26

* More than one organism was recovered from single sample on occasion

must be cleaned with an antiseptic and a detergent and the rubber washer must be carefully inspected. If any cracks are found, the washer is to be replaced. 5. As soon as suitable apparatus is available, the metal top of the humidifier will be put in the autoclave between patients, or after one week, as in point 3. 6. All stored apparatus must be dry. The glass reservoirs must be inverted or covered. 7. Wherever possible, disposable tubing should be used, rather than tubing requiring cleaning. 8. Bacteriological spot checks are to be run at regular intervals.

With reference to the last entry in table 2, the recovery of nonpathogenic mycobacteria in two cases, it should perhaps be emphasized that these were the only two units tested for the presence of Myco. tuberculosis and that they came from another hospital which specializes in the treatment of tuberculosis.

Summary

Systematic investigation of apparatus used in the oxygen therapy section of a large teaching hospital revealed gross contamination in a high percentage. Three main sources of infection were believed to be responsible: (1) contamination of distilled water before it reached the hospital, (2) difficulty in obtaining adequate cleansing of apparatus, and (3) lack of any standard technique specifically designed to prevent contamination.

In view of the lack of previous studies, it is thought that a similar situation may exist in other hospitals. Specific recommendations are made to eliminate the major sources of contamination and include sterilization of the apparatus concerned.

Miss Judith Hiller supplied technical assistance.

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A NEW APPARATUS FOR ARTIFICIAL RESPIRATION

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The ideal respirator should incorporate some sort of control by the patient, so that frequency and depth will be instantly adjusted if the patient begins to breathe spontaneously. If the patient initiates his own breathing, the automatic cycling of the respirator should stop, so as to allow him to do his own breathing without interference. The Pesty positive-negative pressure respirator makes it possible to give artificial respiration by a process of active inflation and deflation at amplitudes and frequencies determined by the operator. No source of electricity is needed, since the required energy is supplied by the compressed air. Mixture of anesthetic gases can be administered in place of compressed air.

Advances in the pathological physiology of respiration have made possible corresponding improvements in apparatus for artificial respiration. Patients with poliomyelitis often need artificial respiration given by such means, but patients anesthetized for surgery, especially under the influence of depressant or relaxant drugs, often also need respiratory assistance in order to maintain normal relations of oxygen to carbon dioxide in the blood. In either type of patient, if the diaphragm or the intercostal or other muscles of respiration are seriously involved, some sort of respirator is a necessity.

The ideal respirator should incorporate some sort of control by the patient, so that frequency and depth will be instantly adjusted if the patient begins to breathe spontaneously. If no provision is made for this possibility, patient and machine are likely to work against each other, and a distressing phenomenon called "bucking the respirator" results. If the patient initiates his own breathing, the automatic cycling of the respirator should stop, so as to allow him to do his own breathing without interference. It is further desirable that the respirator should act not only as insufflator during inspiration (positive pressure phase) but also as aspirator during expiration (negative pressure phase).

This second phase is important, as has been pointed out by Maloney and associates[1]:

> In the group of patients who had some degree of respiratory and/or circulatory inadequacy . . . devices that employ positive pressure only were found to cause a fall in blood

> pressure and cardiac output, sometimes of sufficient magnitude to threaten the life of the patient. On the other hand, the use of a machine employing a negative pressure phase during expiration avoided this circulatory depression, and permitted the patient to maintain blood pressure and cardiac output at more normal levels.

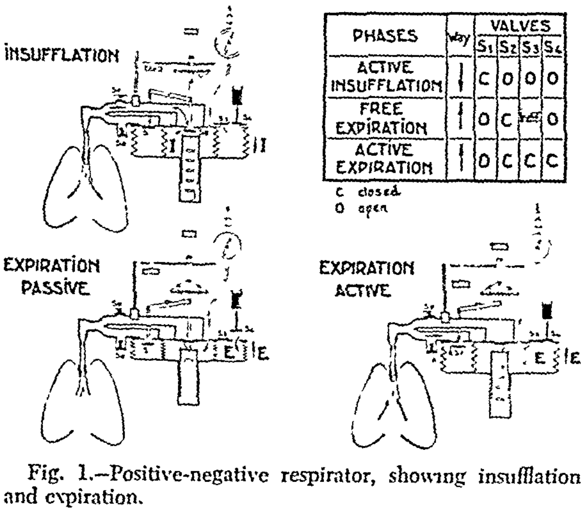
This opinion is shared by Hubay and his co-workers [2]:

> In the closed chest, intermittent positive-negative pressure respiration increases venous return significantly over that measured during positive-atmospheric pressure respiration. The use of a negative pressure phase, between positive pressure lung inflations in the closed chest, is physiological since the mechanisms of increased venous return correspond to those observed with spontaneous respiration.
>
> Positive pressure lung inflation in the closed chest decreases venous return by decreasing the pressure-gradient from extrathoracic to thoracic veins.

These considerations show that the tank respirator, so far from being the only useful means of artificial respiration, can actually be singularly harmful. This has been stated by Bower and others [3]:

> For some time I have been dissatisfied with the performance and action of the standard tank-respirator. In many severe cases it did not permit adequate exchange of oxygen and carbon dioxide during the respiratory cycle, and the pattern of breathing to which the patient was forced to conform did not simulate a normal pattern. Furthermore, in many instances we noted that inability to cough or swallow, laryngospasm, and other factors augmented this inadequate gaseous exchange, preventing the patient from ridding the larynx, trachea, and bronchial tree of excessive amounts of secretion, thus causing additional trouble or death.

It is with these considerations in mind that I present a description of a volume-regulated respirator. Developed on the basis of two years of experiments with dogs, it has been tested in a one-year clinical trial with human subjects.



PHASES	Way	VALVES			
		S1	S2	S3	S4
ACTIVE INSUFFLATION	↓	C	O	O	O
FREE EXPIRATION	↑	O	C	[illegible]	O
ACTIVE EXPIRATION	↑	O	C	C	C

C closed
O open

Fig. 1.—Positive-negative respirator, showing insufflation and expiration.

Description

The Pesty positive-negative pressure respirator makes it possible to give artificial respiration by a process of active inflation and deflation at amplitudes and frequencies determined by the operator. The air-passages within the apparatus are so arranged as to send the air expired by the patient through a spirometer, which measures the volumes concerned and so reveals leaks anywhere in the system. Without affecting the adjustment of amplitude and frequency, it is also possible to vary the relative duration of inspiratory and expiratory phases of respiration. No source of electricity is needed, since the required energy is supplied by the compressed air.

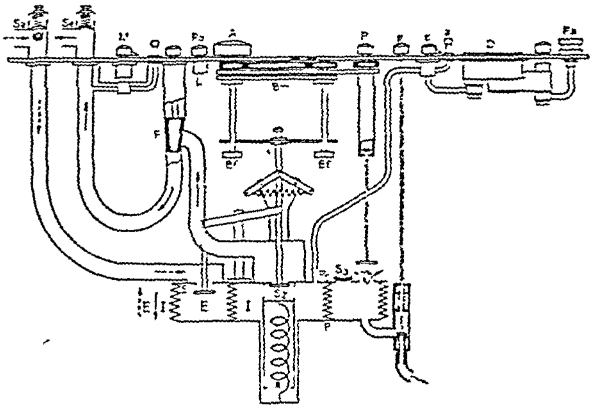


Fig. 2.—Diagram of respirator. *Bm*, movable guard; *A*, regulation screw of movable guard; *Bf*, fixed guard; *F*, braking device on inspiratory circuit; *P*, regulation screw for pause; *p*, device for removing condensed water; *c*, connector cock; *a*, rebreathing bag joint (for manual action); *D*, flow meter; *Ra*, gas in; and *Ro*, regulation cock for aspiration.

The respirator is composed of two concentric or coaxial bellows (fig. 1 and 2, *I* and *E*). These have one wall and two plates in common. The lower plate (*Pi*) is fixed; the other plate (*Ps*) is moveable. The air or gas from the source-tank for inspiration is delivered into the central bellows (*I*). As this bellows expands, it pushes the movable common plate upward. This carries along the outer bellows (*E*), generating a negative pressure and causing the deflation of the patient's lungs. The upward movement of the upper plate (*Ps*) is caused by the compressed air; its return movement is caused by a spring (*R*). The respective volumes of the two bellows are such as to make sure that the outer bellows causes an adequate expiratory movement in the patient.

Valves *S1* and *S2* are so connected with the apparatus that they must close or open in opposition. When *S1* is open, *S2* is shut. When the upper plate rises during the entrance of the compressed air, *S1* opens to permit the patient's expiratory air to be drawn into the outer bellows. When the upper plate returns, drawn by the spring, *S1* closes, *S2* opens, and the air from the inner bellows passes out to insufflate the patient's lungs (fig. 1*A*). The supply of air from the tank is continuous, but the movements of valve *S2* determine the direction of movement of the bellows and are thus responsible for the cycling of the apparatus.

During that part of the cycle when the plate descends in response to the force of the spring and air is passing from the inner bellows to the patient, the air from the outer bellows is being discharged from the exit valve *S3*. This valve is controlled by the difference between the pressure in bellows *E* and the atmospheric pressure. When the plate reascends and bellows *E* and *I* are increasing in volume, the pressure in bellows *E* is negative or subatmospheric. This causes valve *S3* to close. At the beginning of the ascent, the valve *S1* opens suddenly and so establishes communication between bellows *E* and the lungs, which are full of air under positive pressure. Valve *S3* offers a very low resistance to the discharge of the expired air and continues to permit its escape as long as the pressure in bellows *E* exceeds atmospheric pressure.

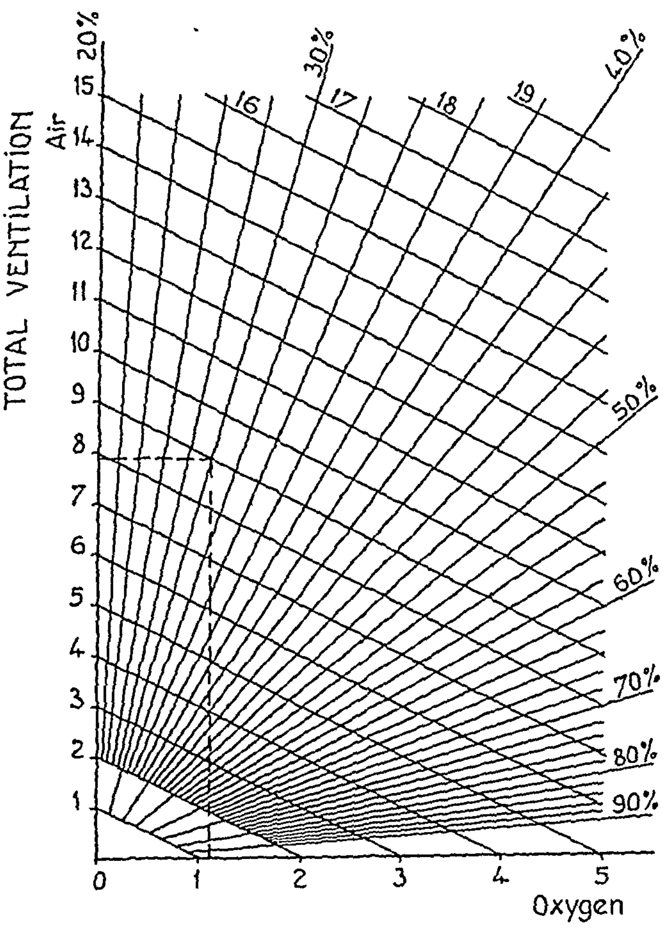


Fig. 3.—Air-oxygen graph for determining rate of ventilation. Abscissa shows flow of oxygen in liters per minute; ordinate shows flow of air in liters per minute; divergent lines show oxygen concentration.

Having permitted a certain amount of expired air to escape, valve *S3* closes. The plate continues to ascend, the pressure in bellows *E* becomes increasingly negative, and the lungs of the patient are actively deflated. It is logical to want to adjust, and indeed necessary to limit, the negative pressure, and that is the function of valve *S4* (fig. 1*B*).

Valve *S4* is suspended above bellows *E* in such a way that the distance between the valve and the bellows in its low position is adjustable. As a result, when the bellows are filling and the plate is moving up, valve *S4* is opened at a certain stage. The exact instant at which *S4* is to open is determined by its setting, and the expiratory or aspirating effect of bellows *E* begins only after valve *S4* is closed. By thus determining the extent of the expiratory action of the bellows, valve *S4* makes it possible to adjust the amplitude and duration of the expiratory phase of respiration (fig. 1*C*).

Further adaptation to the patient's needs is provided for by the existence of a period of inactivity between the active inflation and deflation phases. During this period there is time for the intrapulmonary pressure to approximate atmospheric pressure.

Two other valves, *Sa* and *Se*, will be found on the expiratory and inspiratory circuits respectively. They are safety valves provided with tared springs which prevent the pressures in the lungs from exceeding the limits of safety in either the positive or the negative direction.

Operation

It was noted above that the direction of movement of the bellows is decided by the setting of valve *S2*. Valves *S1* and *S2* are connected by a lever which is governed by a bascule system in such a way that only two positions of equilibrium are possible. The shift from one position to the other is brought about by the striking or impinging of the bascule system against two guards. One guard (*Bf*) is fixed; the other (*Bm*) can be set at various positions. The distance between the two guards determines the amplitude and, consequently, the tidal volume. The amplitude is measured in millimeters of bellows motion. The valve *S4*, set along a millimeter scale, determines the duration of the pause, and the relation, R=pause÷expiratory time, gives the relative duration of the pause.

Application

It is necessary first to decide whether air, oxygen, or a mixture of both is to be used and to determine what rate of ventilation (in liters per minute) is desired. Figure 3 is a nomogram that enables one to set the flow-meters to give a predetermined ventilation rate.

For example, suppose it is desired to give a total ventilation of 9 liters per minute with a mixture having a 30% oxygen concentration. In the graph, one seeks the intersection point of ventilation line 9 with the concentration line 30%. The abscissa of this point is 1.1 (flow of oxygen in liters per minute); the ordinate is 7.9 (flow of air in liters per minute).

Figure 4 is a nomogram that enables one to determine what frequency and amplitude of cycling should be used. The frequency is important, because too fast a rate of cycling decreases the efficiency of alveolar ventilation, while too slow a rate may increase the tidal volume beyond the pulmonary capacity of the patient. In this graph, the abscissa represents ventilation; the ordinate represents rate. The divergent slanted lines show the resultant tidal volume and amplitude value. A scale at the bottom, parallel to the axis of the abscissa, gives the insufflation speed.

For example, suppose a frequency of 18 respirations per minute and an amplitude of 9 mm. is desired. Two heavy lines in the diagram represent this case. They intersect at a point lying on the slanting line which is marked 500 ml. or 0.5 liter, the proper tidal volume. This figure is seen to correspond to an amplitude of 16.5 mm. The additional scale at the bottom, parallel to the axis of the abscissa, shows that a ventilation rate of 9 liters per minute corresponds to an insufflation speed of 2. These nomograms were determined by spirographic measurements and correspond to a respiratory cycle in which the deflation time is double the inflation time.

Conclusions

This positive and negative pressure respirator[4] (fig. 5) with variable pause has been used successfully in various prolonged respiratory inadequacies such as poliomyelitis, polyneuritis, polyradiculoneuritis, myasthenia, toxic coma, and tetanus.[5]

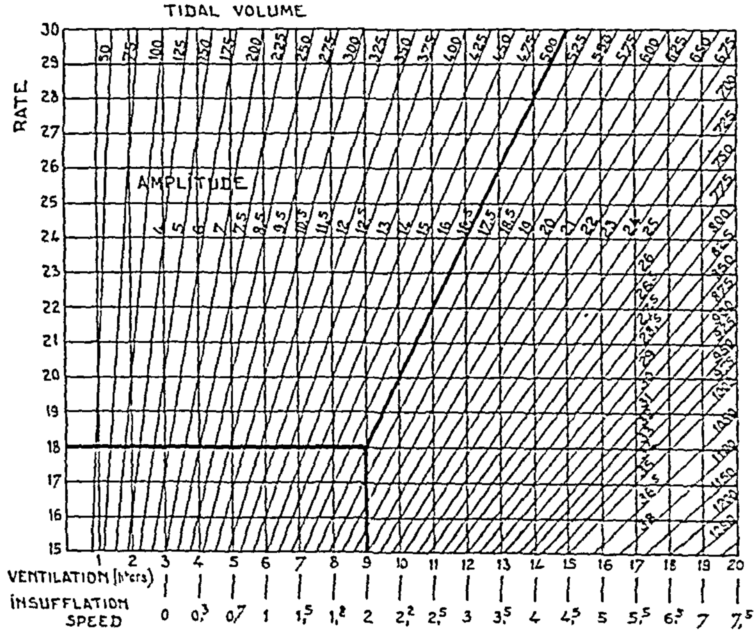


Fig. 4.—Nomogram for determining frequency and amplitude of cycling.

Mixtures of anesthetic gases can be administered in place of compressed air. Huguenard,[6] in particular, used it in 45 cases of major gastrointestinal surgery with cardiopulmonary inadequacy.

The versatility of the apparatus is such as to permit control of (*a*) ventilation per minute, (*b*) tidal volume, (*c*) insufflation speed, (*d*) expiratory pause, (*e*) ventilation rate, and (*f*) positive and negative pressure values. When it is used during surgery, the arterial pulse and pressure are stable, bleeding is diminished (capillary bleeding and vasoplegia caused by hypocapnia), and the venous pressure is likewise diminished. The necessary doses of narcotics are less with use of this respirator. These advantages are attributable to the fact that the apparatus is so precisely adaptable to the patient's needs.

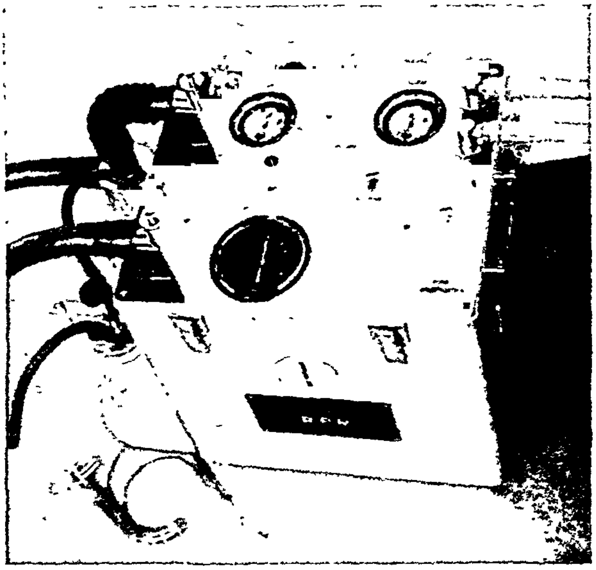


Fig. 5.—Positive-negative pressure respirator.

46, Av. P.-V.—Couturier, 46, Stains (Seine) France.

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RESPONSIBILITIES AND METHODS IN MAINTENANCE OF HOMEOSTASIS IN UNCONSCIOUS PATIENT

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Shock, syncope, coma, and general anesthesia are characterized by the abeyance of various reflexes, some of which are essential for survival. The inadequacy of the patient's responses to conditions that handicap respiration may be especially important. To prevent catastrophes during and after anesthesia the patient's relaxed muscles need assistance, particularly those concerned directly or indirectly with breathing; his position must be such that his airways can be kept free from blood and vomitus, and it may be necessary to remove obstructing material from pharynx or trachea by aspiration. Some patients should have periods of a few minutes at a time in prone or lateral positions lying head down for postural drainage; others who have had operations on the neck may need to be nursed sitting up. Restlessness is not always caused by pain; when it results from hypoxia, the use of narcotics is dangerous because it further depresses the protective reflexes. If prompt and effective treatment is to be available to every patient in emergency, planning is necessary. The equipment must really be at hand, for it is the seconds and not the minutes that count. The requirements include (1) an emergency endotracheal set, (2) an efficient suction apparatus, and (3) apparatus capable of administering oxygen under positive pressure.

The physician is often called in an emergency to take care of patients who have lost their normal defense mechanisms. There are various situations in which the protective reflexes are in abeyance, due to coma, injury, or a number of diseases, and the patient is in grave danger from hypoxia unless something is done to prevent it. Complex treatment is rarely called for. Application of clinical judgment and simple practical measures usually bring about a complete recovery, but lack of prompt intelligent action may mean death or survival with irreversible brain damage.

A good illustration of the type of situation that may arise is given by considering the possible postoperative complications of a routine procedure such as tonsillectomy. For purposes of description, it will be assumed that surgery and nursing care have been mismanaged and that one is called to the recovery room to find a restless young boy lying on his back with a rapid pulse rate, raised blood pressure, noisy labored respiration, and dusky lips and fingernails. On looking around quickly for the simple things needed to deal with this situation, one finds that the crank for tilting the bed is missing, the emergency equipment has been left in the operating room, and the suction apparatus is not working. As the next few minutes pass in frustrating ineffectual efforts to do something helpful, cyanosis deepens and the patients' blood pressure falls; his pulse rate becomes steadily slower and pulse volume weaker; finally, the pupils dilate, his breathing becomes feeble and eventually ceases, and the youngster has died an unnecessary death.

How could this have been prevented? Probably the sequence of events was this. As he was taken from the operating room, he developed partial airway obstruction. The loss of muscle tone from anesthesia resulted in his tongue falling back into his pharynx. The labored breathing brought about by this may have caused enough venous congestion to start some bleeding from his tonsillar fossae, adding further obstruction to his airway. Possibly he may have vomited and have retained some stomach contents in his pharynx. As his cough reflex had not returned, some of this blood and vomitus ran down into his trachea; he became dyspneic, restless, cyanotic, and died from hypoxia.

Prevention of such a catastrophe requires three simple measures. First, his relaxed muscles need assistance; his tongue should be eased forward, and the angles of his jaw pushed up to lift the base of the tongue away from the glottis. Second, his position must be such that he will not suffocate in his own blood and vomitus. Lower the head of the bed and turn him onto his side or, even better, into the semiprone position. Third, he needs aspiration of his air passages to remove the obstructing material if it is accumulating. A soft catheter should be used, with some type of side-opening at its proximal end so that suction through it can be applied

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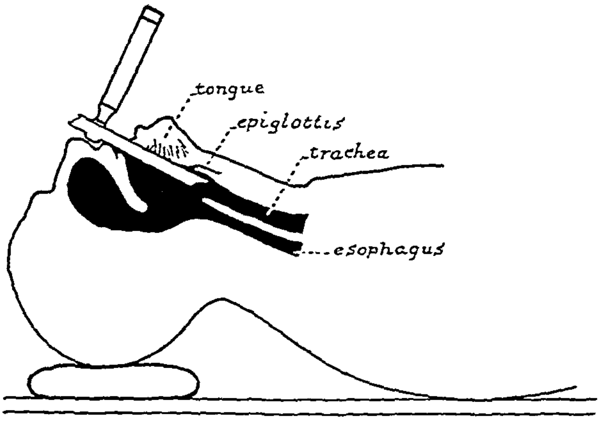
intermittently and damage to the mucous membrane avoided. If he has already aspirated secretions into his lungs, he needs further postural drainage. Turn him from side to side frequently, slap his chest, and encourage him to cough. If he is sufficiently under anesthesia, the suction catheter may be passed into his trachea.

Similar situations may be met with frequently, not only postoperatively but also in the medical wards and in the emergency room. Airway obstruction may be encountered from loss of muscle tone and/or secretions of blood and vomitus occurring in induction and emergence with anesthesia; in coma from head injuries, diabetes, or barbiturate poisoning; in face or neck diseases such as goiter, jaw fractures, and laryngeal edema; in severe pulmonary disease; and in bulbar paralysis. The same principles of treatment apply to all these conditions. Patients may die not from their existing disease but from superimposed respiratory complications giving rise to airway obstruction and chronic hypoxia. Patients with fracture of the mandible, even if they are fully conscious, may become asphyxiated simply because they are unable to keep the mandible elevated and the airway patent. Laryngeal and tracheal narrowing results in typical respiratory stridor. If stridor is not relieved very promptly and conclusively by medical therapy, then immediate tracheotomy is essential. This stridor demands immediate relief. Patients of this type, as well as those who are dyspneic from pulmonary disorders, should be nursed sitting up in order to improve diaphragmatic action and lung expansion. If they have bronchial secretions, they should have periods of postural drainage in prone and lateral positions lying head down, for a few minutes at a time, and sit up in between times. Patients who have had operations on the neck should also be nursed sitting up.

Respiratory distress is often characterized by poor ventilation, either because of instability of the chest wall, as in crush injuries, or because of poor muscular action, as in paralytic disease. In other instances, inadequate oxygen transfer occurs because of pulmonary or cardiac disease. These may all be aggravated by secondary airway obstruction by secretions. Hence, the first line of treatment must include careful clearing of the air passages. This will usually give much improvement, even in the presence of diminished ventilation, as in poliomyelitis. However, if assistance to respiration is still required, a face mask and an anesthetic apparatus may be used for artificial ventilation. When many ribs are fractured, the chest wall may be stabilized by strapping with adhesive tape or by weighting with sandbags. An acute emergency sometimes follows development of tension pneumothorax, either spontaneous or traumatic. In these cases, insertion of a large-bore needle into the pleural cavity may be lifesaving.

Occasionally, these conservative measures are inadequate. Continuous bleeding, as in maxillofacial injuries; the inability to swallow secretions, as in bulbar poliomyelitis; laryngeal or tracheal edema, obstruction, or compression; and retention of bronchial secretions are urgent indications for endotracheal intubation, with either a tube with an inflatable cuff or a pharyngeal pack used to prevent contamination of the trachea. Intubation or tracheotomy is also occasionally necessary in patients with laryngeal edema, or with compression such as may be produced by retrosternal goiter. An endotracheal tube may safely be left in place for 24 hours; after that, tracheotomy is preferable. A tube in the trachea allows tracheotomy to be done without hurry and with less danger of causing hemorrhage or pneumothorax. However, if it is impossible to intubate, then emergency tracheotomy must be done. Both these procedures give good access for bronchial suction and for oxygen therapy, but it should be noted that the ability to cough effectively is lost because positive intrathoracic pressure cannot be built up.



Correct position of patient for intubation or bronchoscopy.

A practical point to be noted is that if the head is extended too far while intubation or tracheotomy is performed, a partial obstruction may be converted into a complete one. The correct position for intubation or for bronchoscopy is shown in the figure. Emergency bronchoscopy is not often indicated. If a major bronchus becomes obstructed and the patient cannot clear it by coughing and postural drainage, then bronchoscopic aspiration is advisable. When a tube or bronchoscope is passed into the trachea, vagal reflexes may result in bradycardia, hypotension, and even cardiac arrest. They should be minimized by giving atropine first, if necessary intravenously, and by using topical analgesia.

Additional Therapeutic Requirements

So far, only the establishment of a patent airway has been considered, and it is emphasized that this necessity takes precedence over all else. Once this has been achieved, it may still be desirable to give the patient additional oxygen. A concentration of 35 to 45% oxygen in the inspired air is the optimum, and for emergency use only a nasal catheter or a face mask should be employed, since the oxygen in an oxygen tent does not reach the optimum concentration until 20 minutes after the tent has been made airtight. When using the nasal catheter, care must be taken not to insert the tip into the esophagus, or the stomach will be inflated. The flow rates required to provide the optimum oxygen concentration are 7 to 9 liters per minute with a face mask with bag, and 4 to 5 liters per minute with a nasal catheter.

If therapy is needed for more than about an hour, it is essential that the oxygen be humidified to avoid drying and crusting of bronchial secretions. A relative humidity of at least 75% must be provided, and there are several humidifiers which will do this. The steam tent may benefit patients who have difficulty in coughing up their secretions. All patients who are mouth breathers or who have tracheotomy or endotracheal intubation must have added humidity because the nasopharynx, where the normal humidification takes place, is bypassed. Positive-pressure oxygen therapy is of great value in pulmonary edema, emphysema, and in certain patients after pneumonectomy. The details of positive-pressure ventilation are important but are outside the scope of this paper. Briefly, the inspiratory pressure should not exceed 20 mm. Hg or the alveoli may be damaged. Also, the positive-pressure phase should take up not more than one-third of the respiratory cycle, and the pressure must fall to zero or below during expiration. High intrabronchial tension transmits pressure to the great veins, causing the cardiac output to fall.

The lessons to be learned from the post-tonsillectomy patient are not yet exhausted. His restlessness might have been wrongly attributed to pain, while in fact it is derived largely from hypoxia. A narcotic drug given to such a patient would be dangerous by further depressing his respiration. Extreme hypoxia will also cause circulatory depression, with rapid pulse rate and low blood pressure, which will respond to improvement in oxygenation.

However, he may have lost sufficient blood to be in genuine shock. Circulatory depression is a predominant sign in traumatic and surgical shock; burns; myocardial depression as in coronary disease, hypoxia, and overdose of drugs, including anesthesia; acute adrenal insufficiency; and acute infections such as peritonitis. It is not necessary to describe the differential diagnosis and treatment of all these conditions. Certain points warrant emphasis. First, if narcotics are to be given to patients in shock, they must be given intravenously in order to be effective, as they are not absorbed from the subcutaneous tissues because of poor circulation. Both these and anesthetic drugs must be used with caution and in small doses. Second, it is obviously better to treat shock early. Pallor, cool skin, and diminishing pulse pressure all precede a fall in blood pressure, and, if treated, hypotension can be prevented. In the anesthetized patient, tachycardia as a sign of impending shock is often absent. Third, it must be assumed that from the moment of injury all digestive and peristaltic activities cease, and patients may have a full stomach many hours after eating and may vomit during the induction of anesthesia.

In the operating room during routine surgery, a number of situations may simulate shock and cause concern until their true origin is realized. For example, the jackknife position, whether the patient is supine or lateral, may cause sudden hypotension associated with kinking and angulation of the patient. Again, the assistant may lean on the patient's neck or chest, causing respiratory difficulties, or, in intrathoracic operations, he may retract on the heart and great vessels, causing sudden disappearance of the pulse. All these are at once remedied by removing the cause. With the patient in the prone position, respiration may be embarrassed unless the abdomen is left completely free; pillows should be placed under the chest and pelvis only. Pressure on the anterior abdominal wall also causes pressure on the vena cava, resulting in engorgement of the lumbar veins, which in such operations as laminectomy makes surgery more hazardous. Air embolism must also be borne in mind as a cause for sudden change in vital signs; it occurs most frequently during intracranial operations.

Occasionally in surgery, the effects of previous drug therapy may be detrimental. If cortisone has been taken within the previous 6 to 12 months for more than a few days, then the stress of surgery may be sufficient to precipitate acute adrenal insufficiency, unless cortisone therapy is continued throughout operation. Tranquilizers such as chlorpromazine and hypotensive drugs such as reserpine and hexamethonium may have their sympathetic blocking action accentuated by anesthesia, and administration of arterenol may be necessary to maintain blood pressure.

All these considerations lead to the conclusion that, if prompt and effective treatment is to be made available to every patient in an emergency, planning is necessary to have all the equipment in readiness. Every emergency receiving room and every place where anesthesia, whether general, spinal, or local, is employed must be equipped with three things: (1) an emergency endotracheal set, (2) an efficient suction apparatus, and (3) an anesthesia or oxygen apparatus capable of administering oxygen under positive pressure. The endotracheal set should contain oral airways, suction catheters, a laryngoscope, tubes of various sizes, and a spray for topical anesthesia. Sets for tracheotomy and for treatment of cardiac arrest should be easily available. It must be emphasized that the equipment must really be at hand, because in all emergency situations it is the seconds and not the minutes that count. A few drugs should also be available on the emergency trays: atropine to dry secretions and block vagal cardiac reflexes, and some vasopressors, one with a predominately cardiac action such as ephedrine or epinephrine and one with a peripheral vasoconstrictive action such as neosynephrine. A barbiturate such as pentobarbital sodium should also be on hand to counteract the toxic effects of local analgesic agents. Should efforts at resuscitation fail and cardiac arrest result, then in these cases it is always worthwhile opening the chest and instituting cardiac massage.

Summary

Postoperative complications may arise when a patient's protective reflexes are abolished, with danger of hypoxia. It is important to maintain the airway by posture, by aspiration of secretions, and, in severe cases, by endotracheal intubation or tracheotomy. The value of being prepared in advance for all such emergencies is preeminent.

ROLE OF INTERMITTENT POSITIVE PRESSURE BREATHING POSTOPERATIVELY

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The frequency of pulmonary complications after surgery has been such as to indicate strongly the need of prophylactic measures, especially against postoperative atelectasis. Among etiological factors to be watched for are narcotics that suppress the cough reflex, dehydration, prolonged immobilization, and constricting dressings. These should be eliminated where possible; additional measures to be taken include chemotherapy, tracheal or bronchoscopic aspiration if necessary, and intermittent positive-pressure breathing (IPPB). For best results, IPPB should be started on the first postoperative day. Three or four treatments daily, each lasting approximately 15 minutes, are recommended. The gas recommended is 40% oxygen with either 60% helium or 60% air. It is delivered under a positive pressure of 15 to 20 cm. water in adults and 10 to 12 cm. water in children, at the rate of 8 to 10 respirations per minute. Adjuvant medication (bronchodilators, antibiotics, expectorants, detergents) can be added as aerosols to the gas. Good results in the prevention of postoperative pulmonary complications are reported in a series of 372 surgical patients, of which 144 underwent thoracic operations.

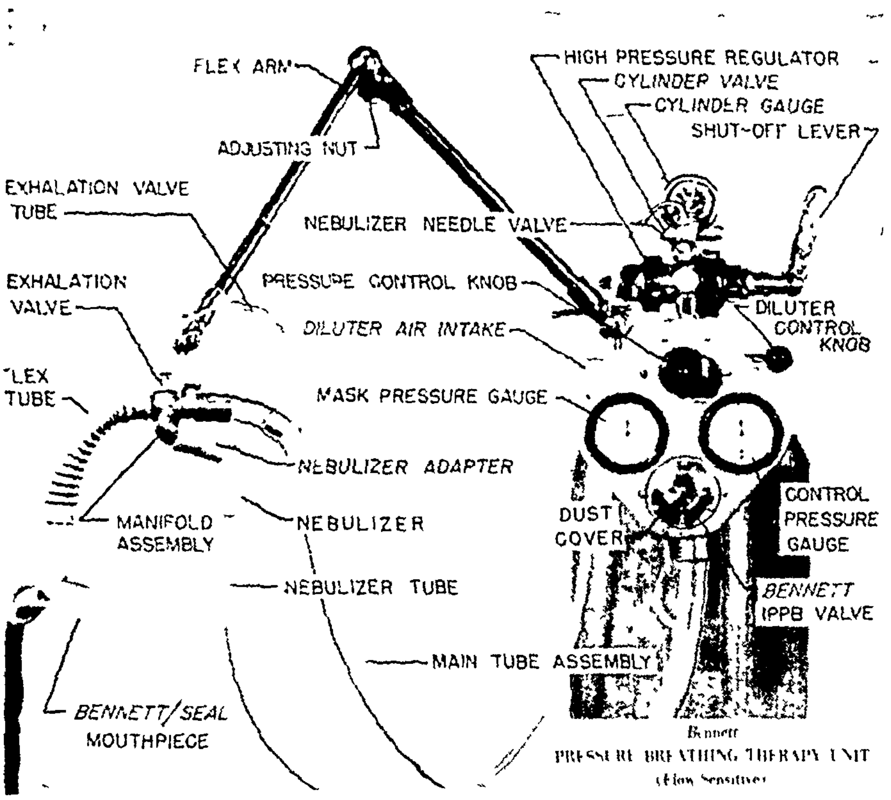
With the increase in magnitude of surgical procedures and the larger number of geriatric patients coming to the surgical theater, the field of respiratory physiology assumes a role of foremost importance. Stevens states in his article on postoperative respiratory complications that the best method of management for acute respiratory problems is optimal prophylaxis. Realizing that this goal is a challenging problem, we recommend the utilization of intermittent positive pressure breathing (IPPB) both as a preventive and as a therapeutic adjuvant. The purpose of this paper is to acquaint the surgeon with the usefulness of intermittent positive pressure breathing in the prevention of postoperative complications rather than to present a statistical review of results obtained with this measure.

Atelectasis

Atelectasis remains the most common of all postoperative complications.[1] Two major varieties of atelectasis exist. One is that caused by paralysis of respiratory muscles, by pleural effusion, or by other factors which decrease effective intrathoracic space. The other type is atelectasis resulting from bronchial occlusion.

Incidence and Etiology.—Various statistics have been reported regarding the frequency of postoperative atelectasis. This condition is clinically significant in 10% of cases when the operative site is the thorax or upper part of the abdomen and in 4% of the cases in which the lower part of the abdomen is the operative site.[1] Segmental atelectasis was found in 94% of patients who developed pulmonary complications after abdominal surgery, as reported by Palmer and Sellick.[2] Swank and Smedal,[3] in a study of young soldiers, reported the incidence of atelectasis and related phenomena induced during stuporous states during deep sodium amytal narcosis. Their startling results showed the incidence of pulmonary complications to be as high as 65%.

In a series of 55 patients in whom partial gastrectomy had been performed, Stringer[4] found that 26 showed abnormal postoperative roentgenographic signs, and, of these, there were 13 with signs of lobular, partial, or massive atelectasis. Douglas[5] incriminates the following causes of atelectasis: (1) suppression of the cough reflex by anesthetic and narcotic agents, so that obstructive elements accumulate in the tracheobronchial tree; (2) dehydration and use of drying agents, so that bronchial secretions become increasingly viscid and more difficult to expectorate; (3) prolonged immobilization during and after surgery; and (4) use of constricting surgical dressings over the lower ribs for abdominal surgery and round-and-round compression dressings still used in operations on the breast.



Pressure breathing therapy unit for administration of intermittent positive pressure breathing combined with simultaneous administration of nebulizer solution of bronchodilator drug. Unit is attached to standard oxygen tank, and treatment is given with patient in sitting or prone position with use of either mouthpiece and noseclip or mask.

Palmer and Sellick[6] report 31 possible etiological factors in the production of postoperative atelectasis; these fall into the following major categories: (1) reduction in bronchial caliber, (2) defective expulsion mechanism, and (3) changes in bronchial secretion.

Diagnosis.—During the first two postoperative weeks, the triad of (1) sudden onset of fever, (2) rapid increase in pulse rate, and (3) diminished breath sounds or bronchial breathing over a lobe or segment of a lobe should alert the clinician to the probability of atelectasis. An x-ray of the chest will usually confirm the diagnosis. Some retraction of the mediastinum and diaphragmatic elevation on the involved side will be further diagnostic proof. Other signs which may prove valuable are deviation of the trachea by palpation to the affected side and limited respiratory excursion on the involved side.

Prophylactic Measures.—Methods of preventing atelectasis should be instituted in all patients who have chronic bronchopulmonary disease and/or decreased respiratory function. These methods include ample fluids, indicated chemotherapy, IPPB, and bronchoscopic aspiration when indicated. Tracheal aspiration is indicated during and immediately after the surgical procedure if secretions have been copious. During the postoperative period, the frequent turning of the patient, inducement of coughing as necessary, prevention of restriction by abdominal binders, regular deep-breathing exercises, and early ambulation is advised.

It is on the latter postoperative measures that we wish to comment in particular. Frequently, some of these are not feasible, for example, coughing by a patient who has undergone herniorrhaphy or standing by a patient with an aortic graft or adrenalectomy in the period immediately after surgery. It is in these patients and in those in whom previous bronchopulmonary disease has been present that we feel IPPB offers the most promise.

What Is Intermittent Positive Pressure Breathing?

IPPB is a technique by which the lungs are actively inflated by means of regulated positive pressure during inspiration and passively deflated to atmospheric pressure during expiration. The expiratory phase functions primarily by the elasticity of the lungs and chest wall.

The apparatus (see figure) is built around a precision flow-sensitive valve. A very low inspiratory suction opens the valve. This is immediately followed by a gradual increase of positive pressure in the mask or mouthpiece to the level set at the pressure-control gauge. At the onset of expiration, the valve closes and the pressure immediately drops to asmospheric level, thus allowing as long an expiration time as is desired without resistance.

The expired air is released through a valve at the top of the manifold, leaving a minimal dead space.

Method of Therapy.—The following plan of treatment is recommended: three to four treatments, each lasting approximately 15 minutes, should be given daily. For best results, the treatments should be instituted on the first postoperative day.

The gas used should be a mixture of helium and oxygen (60% helium and 40% oxygen) if possible. If such a mixture is not available, a mixture of 60% air and 40% oxygen should be used. Newer apparatus now in use are equipped with an air-oxygen diluter that delivers 40% or 60% oxygen mixture as well as 100% oxygen. We advocate the use of helium for the following reasons: 1. Helium is eight times lighter than oxygen and will therefore carry the bronchodilator farther down the bronchial tree, beyond obstructing secretions. 2. Most important is the fact that helium is an inert gas and only slightly diffusible through the alveolar membrane. It therefore remains in the alveoli and bronchial tree for a prolonged period, thus keeping these passages open. In atelectasis the helium passes distal to the secretions and works the occluding substance more proximally in the bronchioles, thereby enabling the patient to expectorate the material more freely. A mixture of oxygen and air is preferable to pure oxygen for the same reason: air contains nitrogen, which is less diffusible than oxygen although more diffusible than helium.

The gas is delivered under a positive pressure of 15 to 20 cm. H_2O in adults and 10 to 12 cm. H_2O in children. It is preferable to begin at a lower pressure and gradually increase to the desired level until the patient becomes accustomed to pressure breathing.

The optimal respiratory rate is 6 to 10 respirations per minute, with a long expiratory phase. The expiration should be passive and not forced, lest it cause collapse of bronchi and expiratory wheezing. Some patients may complain of slight dizziness and paresthesia, and this may be eliminated by decreasing the breathing rate.

The simultaneous administration of aerosol therapy is accomplished by means of a nebulizer attached to the apparatus. One of the following bronchodilators is used: (1) isoproterenol (Isuprel) hydrochloride, 1:20 solution; (2) cyclopentamine hydrochloride and isoproterenol (Aerolone compound solution); or (3) racemic epinephrine hydrochloride (Asthmanefrin). The cyclopentamine and isoproterenol compound is preferred in patients with coronary heart disease and hypertension because it seldom causes coronary vasoconstriction and is less likely to cause an increase in the blood pressure and pulse rate than the other two compounds. Six to eight drops of the bronchodilator is mixed with 15 to 25 drops of water, the larger amount (25 drops of water) used when helium is employed. In lieu of water a detergent, such as Tergemist (aqueous solution of the detergent, sodium 2-ethylhexyl sulfate, 0.125%, with potassium iodide, 0.1%) or Alevaire (aqueous solution of oxyethylated tertiary octylphenolformaldehyde polymer, 0.125%, with glycerin, 5%, and sodium bicarbonate, 2%), may be used in the same quantity. These agents are of particular value in patients with tenacious sputum. Antibiotics have also been given by this method, dosage and kind depending on severity and type of offending organism. Antibiotics should be given only a few days at a time. Particular caution must be exercised in those patients suspected of having allergic diathesis, and use of antibiotic aerosol solutions should probably be avoided in such instances.

Mucus and other secretions are not washed farther down the respiratory tract by the IPPB-aerosol therapy, since the peak instantaneous expiratory flow velocity is greater than the peak instantaneous inspiratory flow velocity.[7] The net result is to work the secretions outward, an expectorant-like action. The duration, frequency of use, and adjuvant medication of IPPB treatment may be adjusted to the particular needs of the patient.

At the Hospital of the Good Samaritan in Los Angeles, IPPB has been used in 372 patients after operation. Of these, 228 were general surgical and 144 thoracic surgical patients. In this series, IPPB was used only when indicated. In the entire surgical group there was a total of 18 deaths, 8 in the general surgical group and 10 in the thoracic surgical group. Four deaths in each group (1.7% and 2.7% respectively) were attributed to or associated with pulmonary complications (average of total group, 2.1%).

An extensive study recently reported by Becker and others[8] revealed that pulmonary complications were responsible for 1,263 deaths in a total of 14,010 patients operated on at the surgical clinic at the University of Giessen, Germany. This figure represents 17.2% of all deaths over a 10-year period (1945-1955) due to pulmonary complications.

Nickel and Renshaw[9] have recently reported their experience in 134 orthopedic patients requiring IPPB either preoperatively, postoperatively, or both. They reported only one case of moderately severe atelectasis, with no deaths.

Summary

The employment of intermittent positive pressure breathing (IPPB) in patients both before and after operation opens a new attack on the problems concerned with the prevention and treatment of atelectasis. Its use is particularly indicated as a prophylactic tool in those patients with chronic pulmonary disease who are to undergo surgery and in those patients who are possible candidates for postoperative pulmonary complications.

The method of IPPB used is as follows: (1) gas mixture of 60% helium and 40% oxygen, (2) three to four treatments for 15 minutes each for five days, (3) positive pressure with 15 to 20 cm. H_2O for adults and 10 to 12 cm. H_2O for children, (4) 8-10 respirations per minute, and (5) aerosol therapy with 6 to 8 drops of a bronchodilator in 15 drops of water.

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HEART SCARE, HEART SURVEYS, AND IATROGENIC HEART DISEASE

EMOTIONAL AND SYMPTOMATOLOGICAL EFFECTS OF SUGGESTING TO ONE HUNDRED SIXTY-TWO ADULTS THAT THEY MIGHT HAVE HEART DISEASE

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One hundred sixty-two individuals who, as a result of a chest x-ray examination made during the course of a tuberculosis survey, were informed that there might be something wrong with their heart were questioned to see if the suggestion that one has heart disease leads to the development of heart symptoms or symptoms of "neuroses." It is not surprising to find persons upset by this procedure, but it is of interest to find that symptoms did not develop to any extent except in persons with preexisting neurocirculatory asthenia. There was no evidence that this procedure precipitated neurocirculatory asthenia (anxiety neurosis, cardiac neurosis, neurasthenia, effort syndrome). These individuals are not necessarily a representative sample of the general population or of patients seen in doctors' offices. The relation of the findings of this study to the concept of iatrogenic heart disease is examined.

Does the suggestion that one has heart disease lead to the development of heart symptoms or symptoms of "neuroses"? Physicians have often discussed this question or reported individual patients in whom this suggestion seemed to be associated with the development or aggravation of such symptoms.[1] The widespread use of disease surveys has caused some physicians to worry about their possible role in upsetting persons and in causing heart symptoms or neuroses. These surveys, designed to detect unknown cases of disease or to determine the prevalence of disease, might conceivably make the public more aware of the symptoms of certain disorders or expose them to the suggestion that they have such disorders. The value and usefulness of such disease surveys could depend in part on their effects, either detrimental or beneficial, on the emotions and symptoms of the individuals studied.

An unusual opportunity to study the possible effects of such a disease survey arose during the Special Heart Survey of the Boston Chest X-Ray Program, in the course of which the suggestion

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was made to a large number of adults that they might have heart disease. We are reporting on the emotional and symptomological effects of this suggestion and its possible relationship to the development of heart symptoms or "neuroses." In addition certain recommendations will be made which may be of help in preventing the undesirable emotional and symptomatological effects of such surveys.

Methods and Techniques

The individuals studied were selected from persons examined in the Special Heart Survey of the Boston Chest X-Ray Program, which was a study of heart disease case finding by means of 70-mm. photofluorographic films. The details of this study have been reported elsewhere by Williamson and associates.[2]

The persons seen in the Special Heart Survey were individuals (1) who on their own volition had a chest x-ray examination made during a tuberculosis survey, (2) whose heart shadow was thought to be abnormal when the x-ray photograph was studied in the Special Heart Survey, (3) who were informed that there might be something wrong with their heart, and (4) who were requested to come to a special clinic for an examination by a cardiologist. A total of 1,154 such persons were examined in the special clinic.

The 162 subjects interviewed in this study were selected by order of registration at the individual sessions of the special clinic. They were interviewed prior to the heart examination and consecutively except when the group waiting to be interviewed became too large. When this occurred, groups of individuals were sent directly for the heart examination and thus were not included in the interview study. The interviewers did not determine the selection of subjects. No individual subject was especially included or excluded by this procedure.

In table 1 the 162 persons interviewed in this study are compared with the 1,154 persons seen in the whole of the Special Heart Survey, with regard to mean age, proportions of men and women, whites and nonwhites, and those with organic heart disease and those without organic heart disease. The 162 persons in this study did not differ significantly statistically from the whole sample of 1,154 in these regards. Seventy-one per cent of our subjects were women. Organic heart disease was diagnosed in 63% of our subjects.

The subjects were interviewed by one of the three authors (51.2% by E. O. W., 34.5% by M. E. C., and 14.3% by C. R. W.). Answers were recorded to 33 questions listed on a mimeographed form. The questions were designed to determine whether the subject (1) had in the past been told that he had heart trouble; (2) had symptoms of heart trouble; (3) had neurocirculatory asthenia (this is considered by the authors to be synonymous with anxiety neurosis, effect syndrome, cardiac neurosis, and neurasthenia);[3] (4) had new symptoms appear or the symptoms of existing disorders become worse; (5) was "upset" by the suggestion that he might have heart disease; and (6) knew what the symptoms of "heart disease" were. With regard to this sixth point, breathing troubles, chest pain, dizziness, faintness, or tiredness were considered to be symptoms of "heart disease." An individual was classed as "upset" when he answered yes to the question "were you bothered, scared, or upset," or when he appeared obviously upset to the interviewer. However, there were only three instances in which an interviewer considered a subject to be upset when the subject did not answer yes to this question. The diagnosis of neurocirculatory asthenia was based on the subject's symptoms and history.[3]

Comparison of the individuals seen by the three interviews (table 2) with regard to proportions of men and women, those over 50 years of age and those under 50 years of age, and those with organic heart disease and those without organic heart disease shows no statisically significant differences. This suggests that the three interviewers interviewed comparable groups, since these data were not dependent on the techniques of the interviewer. If in addition, the three interviewers used similar methods, one would expect that they would get similar results. This proved to be true, for, as is also seen in table 2, the examiners obtained similar results regarding the proportion of individuals who were classified as upset and who were diagnosed as having neurocirculatory asthenia.

TABLE 1.—*Patients in Study Compared with Total Patients in Special Heart Survey*

	Persons Questioned in This Study	Persons Examined in Special Heart Survey	Significance Ratio*
Total no.	162	1,154	
Age (mean)	49.0 yr.	49.1 yr.	0.06
Men, %	29.0	33.1	1.04
Women, %	71.0	66.9	1.04
	100.0	100.0	
White, %	92.6	90.0	1.03
Nonwhite, %	7.4	10.0	1.03
	100.0	100.0	
Heart disease, %	63.0	65.3	0.60
No heart disease, %	37.0	34.7	0.60
	100.0	100.0	

* Significance ratio less than 2.0 suggests that the two groups are not different from one another and that this much difference might occur within the same group by chance, i.e., odds against 20:1.

The subjects in this study were informed in the following manner that they might have heart disease. After having a chest x-ray picture made for diagnosis of tuberculosis in the Boston Chest X-Ray Program, they received a form letter stating there was need for further examination and asking them to make a telephone call to a certain number for an appointment for this examination. On calling this number, they talked with a woman who told them, "Your x-ray is clear for tuberculosis but indicates need for a heart check-up." She then asked them to come to a special clinic for a heart examination and when possible made an appointment at that time. The woman answering the telephone tried to standardize the conversation. In most instances the verbatim details of these conversations were not recorded, but a few verbatim records were made by a third person unbeknownst to the telephoner. In a few instances, an appointment was made without mention of the heart, and occasionally more discussion took place about the heart, x-ray, or details of the heart examination, in order to persuade the subject to come to the clinic.

TABLE 2.—*Comparison of Groups Seen by Three Interviewers**

Factor	Interviewer EOW (83) %	 MEC (56) %	 CRW (23) %
Male	21.7	35.7	39.1
Female	78 3	64.3	60.9
	100.0	100.0	100 0
Under 50 yr.	45.8	50.0	34.8
Over 50 yr.	54.2	50.0	65.2
	100.0	100.0	100.0
Heart Disease	63.8	60.7	65.3
No heart disease	38.2	39.3	34.7
	100.0	100.0	100.0
Upset	43.9	33 9	47.8
Not upset	56.1	66.1	52.2
	100.0	100 0	100.0
Neurocirculatory asthenia	14.6	13.0	13.6
No Neurocirculatory asthenia	85.4	87.0	86.4
	100.0	100.0	100.0

* The three observers interviewed statistically similar groups as regards sex, age, and presence of heart disease and obtained statistically similar results in regard to proportion of persons classified as upset and given diagnoses of neurocirculatory asthenia. Appropriate chi-square and PQ calculations were done and in all instances indicated that the observed differences might occur by chance (odds less than 20:1) and suggested that groups and examining methods were not dissimilar.

The interval elapsing from the time he made an appointment for the examination varied from one day to three months. This interval was eight days or less for 101 of the 147 persons for whom this interval was known. The interval elapsing from the time the individual was told he might have heart trouble to the time he was examined also varied, and was eight days or less for 103 of the 127 persons for whom this interval was known.

Questionnaires were sent to each individual in this study four to six months after the special heart examination in an attempt to learn whether they received a correct impression regarding the presence or absence of heart trouble, were upset or were reassured by what they were told, were glad they came to the clinic, or had any criticism to make about the Special Heart Survey. Replies were received from 90, or 55.6%, of the 162 subjects. In some instances answers to one or more of the questions were omitted or were such as to suggest that the question was not understood. Thus complete conclusions cannot be drawn from this questionnaire information.

The data were analyzed according to standard statistical methods, using the standard error of the difference between means, the standard error of the difference between proportions, and the chi-square test with the correction of Yates for small numbers.[3] In this paper, a difference is considered to be statistically significant if the odds against its being a chance occurrence are 20:1 or greater, i. e., a significance ratio of 2.0 or greater.[3]

Results

The data from the interviews were analyzed with special attention, first, to the proportion of persons upset and the factors associated with this reaction; second, to the development of symptoms; third, to the aggravation of symptoms of preexisting disease; and, fourth, to the person's general information about the symptoms of heart disease, in addition to other factors. The information from one questionnaire was very incomplete because the subject was deaf and understood English poorly. Most of the results are based on the 161 questionnaires with adequate information. A brief summary of the answers to the follow-up questionnaire is included.

Of 161 persons, 66, or 41%, were classed as upset (table 3). The suggestion that they might have heart disease upset a larger proportion of women (51.8%) than men (14.9%), a larger proportion of the persons from 11 to 49 years of age (58.1%) than the persons of 50 years or over (26.4%) and a larger proportion of the persons who in the past had not been told they had heart trouble (46.2%) than the persons who in the past had been told they had heart trouble (29.6%). These differences in proportions are statistically significant, the significance ratio decreasing from 4.32 for sex, to 4.06 for age, to 2.02 for previous knowledge about the presence of heart disease. When all three factors were present, i. e., when the subjects were women, were young, and had not been told in the past that they had heart disease, 76.9% were upset. When all three factors were absent, i. e., when the subjects were men, were old, and had been told in the past they had heart disease, none were upset.

TABLE 3.—*Factors Related to Being Upset*

Group	No.	% Upset	Significance Ratio*
Entire sample	161	41.0	
Women	111	51.8	
Men	47	14 9	4 32
Age 11-49 yr.	74	58.1	
Age 50+ yr.	87	26.4	4 06
Not previously told had heart disease	106	46 2	
Previously told had heart disease	54	29.6	2 02
Neurocirculatory asthenia	22	68 2	
No neurocirculatory asthenia	139	36.7	2.79

* Significance ratio greater than 2 0 suggests that the observed difference is larger than might occur by chance (odds 20:1 or greater).

The subjects were divided into eight groups (table 4) on the basis of these three factors, and these eight groups were arranged in descending order of the proportion of upset persons in each group. It is seen that a greater proportion of women were upset than were men, regardless of the other two factors; a greater proportion of young women were upset than old women, and the same of men regardless of their previous knowledge about the presence of heart disease; and, finally, a greater proportion of persons who in the past had not been told they had heart disease were upset than persons who in the past had been told they had heart disease, provided they were of the same age and sex. The number of persons in each of the eight groups is generally too few to permit useful statistical analysis. However, the fact that the data are consistent with clinical and common-sense impressions suggests that sex, age, and previous knowledge about the presence of heart disease are factors in being upset in that order of importance.

Of the 22 persons with neurocirculatory asthenia, 15 or 68.2% were upset as opposed to 36.7% of those persons without this disorder. The proportion of persons upset was at its most extreme (100%) when this fourth factor, neurocirculatory asthenia, was present in the young women without previous knowledge of heart disease. The 46 persons who delayed eight or more days before making an appointment and the 24 persons who were not examined for eight or more days after being told they might have heart trouble did not have a greater or lesser proportion of upset individuals than did those who did not experience this delay. Thirty-nine of the 66 persons who said they were upset gave the following information as evidence of this: symptoms had appeared or become worse in 13 persons, 13 had called their doctor, 10 had "trouble in sleeping," 7 had crying spells, 8 had decreased their activity, 3 had "trouble in eating," 2 had stopped smoking, and 2 had counted their pulse.

In 13 individuals (8.1%) cardiovascular symptoms appeared or the symptoms of previously existing disorders were aggravated. In 10 of these persons, 9 with neurocirculatory asthenia and 1 with angina pectoris, the symptomatology of the disorder increased. Of the remaining three individuals, two who previously had no symptoms developed awareness of heart beat, while the third, who previously had been bothered by some of the symptoms of neurocirculatory asthenia, developed more symptoms and had "probable" neurocirculatory asthenia, in our terminology,[3] at the time of the interview. Of the 22 persons with neurocirculatory asthenia, 9, or 40.9%, noted an aggravation of symptoms or the appearance of new ones in contrast to only 2.2% of those persons without neurocirculatory asthenia. Thus, while a large proportion (41%) of the individuals in the study were upset, only a few (8.1%) noted the development or aggravation of symptoms. There were no definite instances of clear-cut neurocirculatory asthenia developing in individuals who had not previously had this disorder.

Neurocirculatory asthenia antedating the present study was found in 22, or 13.7%, of 161 subjects. This is a higher prevalence than that reported for samples of the general population in the same area where it averaged 4.7%.[4] However, in another community heart survey at Framingham, Mass., Kannel, Dawber, and Cohen found the prevalence of neurocirculatory asthenia was 11.6% of 1,214 subjects. It is possible that some health surveys attract a disproportionate number of patients with neurocirculatory asthenia (anxiety neurosis). This prevalence is close to that found in this study.

Only a few of the first 69 subjects in this study mentioned any heart symptoms. Therefore it seemed of interest to ask the remainder of the subjects, 93 in number, about their knowledge of heart symptoms. This was because we wondered if the suggestion of heart disease would not lead to heart symptoms unless the subject were educated in the symptoms of "heart disease." Thirty of these persons could not name a single symptom of heart disease. The 93 persons knew a mean of only 1.03 symptoms. These people were generally not well aware of the common symptoms of heart disease.

TABLE 4.—*Relation of Sex, Age, and Having Previously Been Told or Not Told One Had Heart Disease to the Proportion of Individuals Upset*

Sex	Age (Yr.)	Previously Told About Heart Disease	Size of Group*	No. Upset	% Upset
F	11-49	No	39	30	76.9
F	11-49	Yes	14	6	42.9
F	50+	No	38	14	36.8
F	50+	Yes	22	8	36.4
M	11-49	No	13	4	30.8
M	11-49	Yes	7	2	28.6
M	50+	No	16	1	6.3
M	50+	Yes	11	0	0.0

* Two persons were omitted, one because it was not clear whether he had previously been told about heart disease, other because deafness interfered with answer.

Of the 87 persons who answered the question "What did the doctor at the Special Clinic tell you about your heart?" 75.8% had received a reasonably correct impression about the presence or absence of heart trouble, 11.5% had an incorrect impression, and 12.7% did not know. Of these 87 persons, 31.7% were not informed at the time of the clinic examination whether they had heart trouble and were left in doubt for varying periods of time until they or their physicians received a report. Five of these persons stated that they never received any information about the results of the examination. Of this group, 92.6% were glad of the opportunity to have the examination, while 7.4% made some adverse comment, generally having to do with delay in receiving information about the results of the examination, as stated before. The results of this questionnaire were not wholly conclusive.

The subjects were questioned concerning what was upsetting to them about being asked to come in for examination. They were also given an opportunity to express their fears, if any, of tuberculosis as compared with their fears, if any, of heart disease. Some of the patients' own answers throw some light on their feelings. Excerpts of verbatim statements follow.

Statements of patients who were upset: "can't have any more children if heart is bad," "couldn't sleep," "might have to quit job," "might die," "might not be able to roller skate," "thought it was tb (tuberculosis) . . . ready to go to Adirondacks . . . would have to leave college," "getting more rest since got the letter," "thought would be sent away for tb," "was scared to death for fear I had tb . . . when I found it was my heart, I danced up and down I was so happy," "thought it tb . . . couldn't have children or grandchildren to play with."

Statements of subjects who were not upset: "thought it might be due to a tight girdle," "thought it was because I wore a dress with spangles on it," "not upset . . . knew about murmur," "not upset . . . heart is a good way to go out," "it's quicker" (i. e., a cardiac death), "knew I had a murmur," "had a heavy cold when the x-ray was taken and thought something might show," "reason not frightened because I recently passed an insurance examination," "thought it was a mistake."

The initial card to the patient did not make clear whether heart disease or tuberculosis was suspected. Most patients expressed the opinion that they preferred heart disease to tuberculosis, given a hypothetical question as to preference. They felt that heart disease had good treatment these days and that tuberculosis implied being sent away, being separated from family and children. Many patients thus expressed a fear of tuberculosis because they might be sent away and separated from family and children; fear of heart disease because they believed it led to sudden death.

Comment

The individuals interviewed in this study are a good representative sample of those persons examined in the Special Heart Survey Study. They are not necessarily a representative sample of the general population or of patients seen in doctors' offices. Thus the findings in this study may not apply to other groups of people chosen in a different manner. One suspects that persons who are worried about their health and also those having symptoms would be more apt to have a chest x-ray study and agree to come in for an additional examination than would symptom-free, unworried persons. The high prevalence (13.7%) of neurocirculatory asthenia (anxiety neurosis, effort syndrome, neurasthenia, nervous exhaustion) in the group interviewed is in keeping with this belief.

Persons were classified as "upset" when they said they were upset. No attempt was made to assess the degree to which they were upset because no reliable method is known by which this may be quantitated. The suggestion, implied by the telephone call, that the individual had heart disease was obviously an upsetting one. It did not come directly from a physician but carried the weight of medical authority. How this differs in effect from a suggestion coming directly from a physician is not known.

It was not surprising to find persons upset by this procedure, but it was of interest to find that symptoms did not develop to any extent except in persons with preexisting neurocirculatory asthenia. Nor was there evidence that this procedure precipitated neurocirculatory asthenia (anxiety neurosis, cardiac neurosis, neurasthenia, effort syndrome). The internal from the time the individual was told he might have heart disease to the time of the interview was generally not many days. How soon one would expect symptoms of neurocirculatory asthenia to develop is not known. The data from the literature are not adequate to tell exactly what the incubation period is between medical words and aggravation of symptoms, but the implication seems to be that the effect is probably immediate. Being upset, however, did not seem to be related to the length of interval between stimulus, the telephone call, and our examination and interview. The follow-up questionnaires did not supply reliable information concerning the possible later development of symptoms or neurosis. Aggravation of preexisting neurocirculatory asthenia certainly occurred. This is similar to observations on the clinical course of the disorder.[4]

It was interesting to find that these persons knew little about the symptoms of heart disease. Persons who, through long periods of hospitalization or through frequent interviews with doctors, have had a chance to learn the symptoms of heart disease might respond differently than this group who had little knowledge about heart symptoms. It is possible that patients exposed to litigation, pension procedure, or unwise health propaganda might catch a few symptoms.

It is of psychological interest that more women were upset than men and that more younger persons were upset than were older persons. If one wished experimentally to upset people, then this study suggests that young women who had never been told they had heart trouble are the subjects of choice. If one wished to choose the group least likely to be upset by this suggestion, one should pick older men who have already been told they have heart trouble. This fits with a popular belief that women are more easily upset than men. The explanation of this may be actually as simple as some of the young women have stated it above, i. e., that sickness would interfere with their home life, having children, and being able to remain at home and care for them.

There are a number of reports[1] which suggest that doctors' words or advice may lead to an undefined condition called "iatrogenic heart disease." Probably this loose term usually implies that a previously well person develops a number of symptoms, which include palpitation, chest pain, dyspnea, nervousness, and faintness. There are other possibilities, however: (1) that the doctor's words have given the patient the belief that he has heart disease when he really does not, (2) that the patient's inactivity or incapacity results from the doctor's advice; or (3) that a previously existing condition such as anxiety neurosis (neurocirculatory asthenia) is made worse or the patient's incapacity from neurocirculatory asthenia is made worse by the doctor's words. Over a period of 30 years there have been published a number of papers which discuss the general subject of "iatrogenic heart disease." Fourteen of these (table 5) give some relevant data about 44 patients. In only 4 of these 44 cases is it stated that the patient had no symptoms before seeing the doctor. Thus when the literature actually gives case reports (table 5) there do not seem to be many cases in which heart symptoms or neurocirculatory asthenia are caused by doctors' words or advice in symptom-free persons. However, the clinical data from the literature suggest that preexisting symptoms or incapacities are increased. The data in the literature (table 5) are thus in close agreement with the results of our study.

TABLE 5.—*Evidence from the Medical Literature for "Iatrogenic" Heart Disease or Symptoms*[*]

Author	Yr.	Cases, No.	Cases with Relevant Data	No Symptoms Before Seeing Doctor[†]	Worse After Seeing Doctor[‡]
Viko	1925	23	1	1	1
Kilgore	1929	1	1	1	1
Connor	1930	6	6	1	2
Ollle	1941	15	15	0	0
Wood	1941	59	1	0	1
Weiss and English	1943	3	3	0	?
Douglas-Wilson	1944	14	0	0	0
Auerback and Gliebe	1945	4	4	0	1
Drake	1948	1	1	0	0
Goldwater, Bronstein, and Kresky	1952	175	0	0	?
Weinberg	1953	1	1	0	?
Arenberg	1954	7	7	0	?
Grytting	1954	2	2	0	2
Long	1955	2	2	1[§]	1

[*] Reference 1.

[†] Clearly stated that patient had no symptoms before seeing doctor.

[‡] Time elapsing between medical words and aggravation of symptoms was noted in three cases and was short in all three.

[§] Personal communication to the authors.

There is little evidence that "iatrogenic heart disease" as usually understood (the doctor's words causing a symptom complex in previously healthy persons) actually exists. Probably the disorder described under this term is usually neurocirculatory asthenia, hysteria, or depressive disease which may have been aggravated by a doctor's words. These latter conditions are believed to be aggravated by a variety of upsetting situations[4] one of which may well be careless or thoughtless practices of a physician. The data in the literature and the results of this study support the latter idea about so-called iatrogenic heart disease, but they do not support the popular misconceptions concerning its nature, frequency, or etiology. It would be our recommendation that the term "iatrogenic heart disease" be dropped. Dropping this inaccurate term does not mean condoning careless or thoughtless words or practices of physicians or others interested in health and disease. Such practices are never acceptable and may well aggravate neurocirculatory asthenia, hysteria, or depressive disease. Hart[5] also examines critically the concept of iatrogenic heart disease and points out that patients have symptoms before seeing the physician and also that in most cases no one really knows what the physician actually told the patient.

The interviews and answers to the follow-up questionnaire suggested that the following features of the survey were special sources of worry to the subjects and certain recommendations seem indicated. 1. The original notification that the subjects received in the mail gave no indication of what was thought was wrong, and many persons assumed it was tuberculosis. A statement on the notification letter to the effect that there was no tuberculosis suggested by the chest x-ray might cause less alarm. 2. Some subjects received their notifications on Friday and had to wait until the following Monday before finding out what was suspected to be wrong in their chest x-ray, and they reported spending an anxious few days. This could be avoided by having someone answer the appointment telephone on week-ends and holidays if disturbing messages are sent out just before those times. 3. Subjects occasionally received alarming impressions from the telephone conversation. Careful instructions to the person answering the appointment telephone might avoid some of these impressions. 4. Every attempt should be made to examine the subjects as soon as possible once they are given the "heart suggestion." 5. Subjects who were not informed about the results at the end of the examination had to wait until their own physicians received a report before learning of the results, and their own physicians occasionally failed to inform the subjects. It would seem to be the responsibility of the examining physician at the special clinic to cooperate with the family physician in informing the subject about the results of the examination. If for some reason this cannot be done, the subject as well as his physician should receive a general report. Of course, unnecessary medical details should not be given to the patient.

Conclusions

From observations on 162 adults in a community survey to whom it had been inadvertently suggested that they "might have heart disease," it was concluded that although such a suggestion seemed to upset and frighten almost half of the persons it did not seem to lead to symptoms of heart disease, neurocirculatory asthenia, or "neurosis" in persons previously free of such symptoms. However, a few patients with past symptoms of neurocirculatory asthenia (anxiety neurosis) or angina pectoris showed aggravation of symptoms of those conditions. It was concluded that such "suggestions" resulting in "heart scare" might aggravate the symptoms in some cases of previously existing disease.

It was of interest that the highest proportion of persons who were upset by the suggestion of heart disease were women, 51.8%; younger persons, 58.1%; and persons not previously told they had heart disease, 46.2%. The combination of persons young, female, and not "previously told" yielded the highest proportion of frightened persons, 77%. Adding neurocirculatory asthenia made this proportion even higher. It was concluded that these categories of human beings are more easily upset than others.

On the basis of patients' statements and general impressions it seems advisable, in future surveys, if only from the standpoint of courtesy and of avoiding upsetting people, to observe the following suggestions: 1. Once the question of suspected disease is brought to a patient's attention, the patient should be examined soon. Meanwhile he should have the opportunity, including weekends, to reach the office by telephone for possible explanations or reassurance. 2. Appointments or other personal information should not be sent on postal cards. 3. Reassuring statements that there is no disease or of the nature of the disease should be given as soon as possible. 4. No one giving information should be mysterious or evasive. 5. Unnecessary information about symptoms of disease should not be given to the general public.

There was no evidence, from this study, that any [illegible], either medical or psychiatric, follows a heart survey or that patients are dissatisfied with such studies. The data from this study support the literature on "iatrogenic heart disease," to wit, the symptoms and disability of patients with previous heart or nervous disease may become aggravated by a doctor's words, but there is little or no evidence that a doctor's words create symptoms or disease in individuals who were previously free of symptoms or disease.

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SUGGESTION ABOUT GOUT.—A study on red blood cells from galactosemic individuals revealed in a striking way that it was indeed the Gal-I-P transuridylase which was defective and that the other members of the chain were present. The same relationships were later demonstrated in liver biopsies; hence congenital galactosemia represents another example of a metabolic block. There may well be family diseases which may be more involved than a simple metabolic block. For instance, Stetten has found that patients with gout make uric acid from glycine much more readily than can be explained by the nucleotide pathway. He has therefore suggested that gout may represent a revival of the uricolytic pathway of birds. Perhaps gout is to be considered an atavism to the bird or reptile stage, an unhappy back-mutant to the "wild type" without the ability to live a wild life because the individual does not possess an avian kidney.—H. M. Kalckar, M.D., Some Considerations Regarding Biochemical Genetics in Man, *Perspectives in Biology and Medicine,* vol. 1, no. 1, 1957.

CLINICAL NOTES

MULTIPLE ANTIGEN FOR IMMUNIZATION AGAINST POLIOMYELITIS, DIPHTHERIA, PERTUSSIS, AND TETANUS

I. RESPONSE OF INFANTS AND YOUNG CHILDREN TO PRIMARY IMMUNIZATION: PRELIMINARY REPORT

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The use of triple antigen (diphtheria, pertussis, and tetanus combined, or DPT) in pediatric practice is well established, and its efficacy has been reviewed and discussed by Edsall[1] and Ipsen and Bowen.[2] With the accepted schedules of four-to-six-week intervals between inoculations, there has been good response to each of the three antigens in combination even when immunization is started at a very early age.[3] During 1956 the attack rates for paralytic poliomyelitis were highest in one-year-old children,[4] thereby also indicating the need for early poliomyelitis immunization. The widespread use of killed trivalent poliomyelitis vaccine in older children has been amply justified and the vaccine shown to evoke a response in infants.[5] On this basis poliomyelitis immunization of infants has been advocated[6] and the possibility of incorporation of the poliovirus antigens into DPT has aroused considerable interest. Response of infants to pertussis vaccine or DPT and poliomyelitis vaccine, physically mixed just prior to administration, or injected simultaneously into separate sites, has been reported,[7] as have laboratory studies showing animal response to mixtures.[8] However, difficulties in formulation and incompatibilities, together with the desirability of keeping the dose volume small (less than 1.5 cc.), have delayed the preparation of a desirable multiple-antigen product. As soon as these problems were resolved, the two lots of Quadrigen (combined DPT-poliomyelitis vaccine, aluminum phosphate absorbed) used in this study were prepared.

Method

The poliomyelitis vaccine components were from two lots of vaccine prepared by the formalin-ultraviolet irradiation procedure[9] and previously released for commercial distribution by the Division of Biologics Standards of the National Institutes of Health (NIH). Purified and formalin-treated diphtheria and tetanus toxoids containing purified and recrystallized benzethonium chloride (Phemerol), 1:40,000, as preservative were specially prepared. An available experimental lot of inactivated pertussis suspension prepared without preservative was employed. Concentrates of the component antigens were used so that a fully effective dose of each would be contained in the desired 0.5-cc. inoculum volume. The components were adsorbed on Holt-type aluminum phosphate adjuvant[10] so that a final concentration of 2 mg. of mineral carrier per 0.5-cc. dose would result. Thus, by use of benzethonium chloride as the preservative, concentration of the antigens, and incorporation of a mineral carrier, a potent and compatible product was achieved.

The potency of each component in the final vaccines (Quadrigen, lots B-090890 and B-090891) was determined by the standard animal test procedures prescribed by the NIH. With the exception of pertussis, each individual antigen, after combination, met or exceeded minimum requirements (see table) established for monovalent vaccines. The parent pertussis suspension, which had been stored for over one year, without preservative, had diminished in potency, and retests showed that the below-standard potency was not due to the method of preparation or the combination with the other antigens.

The subjects in which the vaccines were studied were children under current supervision in the child health clinics conducted by the Detroit Department of Health. Children, ranging in age from 2½ months to 5 years, were alternately assigned to receive one of the test vaccines; 298 contributed preinoculation blood specimens.

It was decided for this preliminary trial to follow the DPT immunization schedule in regular use by the health department to determine whether adequate response to poliomyelitis antigen could also be elicited by this customary procedure. Accordingly, all children received three monthly intramuscular 0.5-cc. inoculations of Quadrigen, and those starting the series prior to the sixth month of life were given four. Blood specimens were obtained at the time of each inoculation and one

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From the City of Detroit Department of Health (Drs Barrett, Molner, and Anderson) and Parke, Davis and Company (Drs Timm, Wilner, Carnes, and McLean).

month after the final injection. A satisfactory series of serums for determining antibody response to the three doses was obtained from all children (224) who completed the three-dose schedule. Only 46 children of the 120 eligible for the fourth dose contributed a fifth blood specimen one month later. Special effort was made to obtain enough blood at each sampling to permit testing for poliovirus antibodies (types 1, 2, and 3), diphtheria and tetanus antitoxin, and pertussis agglutinin. When insufficient serum was obtained, priority for test was assigned in the order listed. The poliovirus neutralization antibody determinations were made in monkey kidney tissue cultures in disposable plastic panels.[11] Tests for diphtheria and tetanus antitoxin were performed according to accepted procedures,[12] and response to the pertussis antigen was determined by tests for specific agglutinin.

Animal Potency Test Results, by Standard Government Methods, with Quadrigen

Components	Quadrigen Lot B-090890	Quadrigen Lot B-090891	Minimum Requirements
Poliovirus, type* 1	1.15	0.37	0.29-0.86
2	1.39	1.48	0.25-0.75
3	0.24	0.29	0.16-0.48
Diphtheria†	3	2+	2
Tetanus‡	4(5 wk.)	3(5 wk.)	2(by 6 wk.)
Pertussis§	5.4	5.4	12(range 8-36)

* Monkey antibody response factors. Additional Standards: Poliomyelitis Vaccine, Federal Register, p. 4922, paragraph 73-100, July 3, 1956.

† Guinea pig antitoxin units per milliliter. Minimum Requirements: Diphtheria Toxoid, 4th revision, Federal Security Agency, National Institutes of Health, Bethesda, Md., March 1, 1947.

‡ Guinea pig antitoxin units per milliliter. Minimum Requirements: Tetanus Toxoid, 4th revisions, Federal Security Agency, U. S. Public Health Service, National Institutes of Health, Bethesda, Md., Dec. 15, 1952.

§ Mouse antigenic units per 1.5 ml. (Quadrigen). Mouse antigenic units per total dose (minimum requirements). Minimum Requirements: Pertussis Vaccine, 1st revision, Federal Security Agency, U. S. Public Health Service, National Institutes of Health, Bethesda, Md., Oct. 31, 1952, amendment 2.

Results and Comment

Intercurrent Illness and Reactions.—Mothers were questioned at each clinic visit and asked to report all illnesses or "reactions" by telephone. Physicians were also alerted to examine patients at each visit for evidence of local tissue response at the site of previous injections. These methods, of course, were not completely accurate in determining the frequency or intensity of reactions during the first 48 hours following the antigen injections.

During the course of the trial, in which a total of 851 inoculation exposures accumulated, there were 126 reported instances of unrelated illnesses—mostly upper respiratory infections or the common diseases of childhood—and 30 reported instances of reactions possibly due to the immunization procedure. Tenderness at the site of injection or leg soreness was reported in 16 instances; however, the femoral venipuncture procedures may have been contributory. Ten instances of fever were reported by mothers within 48 hours after an inoculation. There were four instances of reported rash: one a vesicular pruritic type observed after the third dose (a similar history was obtained after the second dose in this same child); another, an urticarial type of reaction following the second injection; two other instances were reported by mothers who gave a history of rash in their individual children.

On the decision of the clinic physician, 13 children were dropped from the study, 7 because of respiratory infections, 4 due to exposure to scarlet fever, 1 because of an urticarial reaction following injection, and 1 because of vasomotor instability following venipuncture. Another 61 were voluntarily withdrawn from the study by their parents. Over 75% of the children completed their prescribed course of primary inoculations.

Preimmunization Antibody Status.—The 298 preimmunization blood specimens were tested for diphtheria and tetanus antitoxin levels, pertussis agglutination titers, and poliomyelitis neutralizing antibodies. Of these, 52 serums showed diphtheria antitoxin levels of 0.01 units per cubic centimeter or greater, with 19 of these from children over 6 months of age. Fourteen of the 22 who had greater than 0.1 units per cubic centimeter of tetanus antitoxin were over six months of age. None of the 298 preimmunization blood specimens contained significant pertussis agglutination titers. Ninety-four of the children had triple-negative reactions for poliomyelitis; that is, they had no demonstrable antibody titers (less than 1:4) against the three types. By types, 203 were negative to type 1, 141 to type 2, and 224 to type 3. Since the half-life of

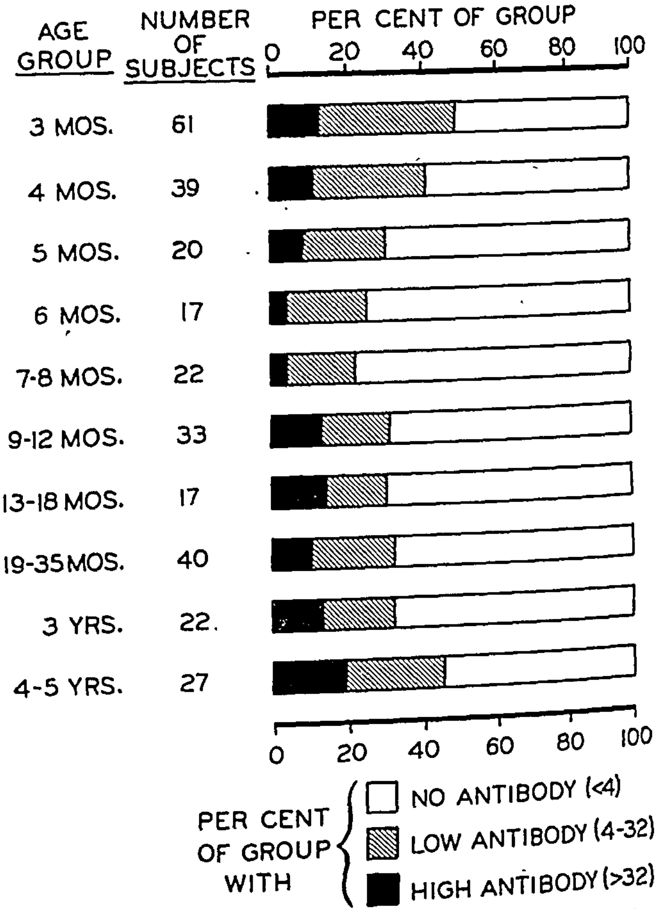

Fig. 1.—Composite preimmunization distribution of poliovirus antibody by age groups among 298 children.

poliomyelitis antibody has been reported to be one and one-half months,[13] most of the demonstrable antibody in the younger group may have been passively acquired from the mother (approximately half of the children in the study were 6 months of age or younger).

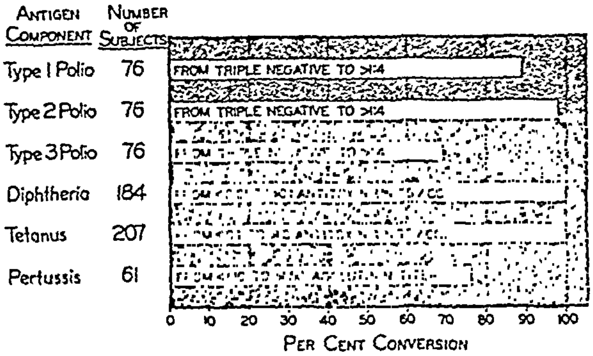

Fig. 2.—Conversion rates for component antigens after primary immunization schedule.

When the percentages of children without antibodies for each type of poliovirus were compared on the basis of age groups, in each instance the peak level of negative reactions was found at 7 to 8 months. In general, passive antibody levels were most prevalent for type 2, and subsequent exposure seemed to occur at an earlier age, with active antibody making its appearance sooner. Exposure to type 3 was apparently not as early in this group of children, and passive antibody was also observed less frequently. At age 7-9 months 98% were without antibody to type 3. Type 1 was intermediate in passive antibody level and probable time of exposure. A composite summary of the incidence data for the three serologic types is presented in figure 1. This chart illustrates the shifting antibody pattern with age as passive maternal antibody is lost and antigenic experience through natural exposure is acquired. Up to 7 or 8 months of age the incidence of demonstrable antibody decreases progressively, while in the older children the incidence increases with age as could be expected through chance exposures to poliomyelitis antigens. It is of interest that this change in the trend of antibody pattern is correlated with the increasing independent activity of the child after 6 months of age.

Response to Primary Immunization.—No significant difference was seen in response to the two lots of Quadrigen studied, either in antibody levels or in conversion rates. Therefore, the results from the two preparations have been combined for this evaluation. Conversion rates one month after completion of the primary series of three 0.5-cc. inoculations (or four if a final blood specimen was obtained) are given in figure 2. Of the 76 subjects with triple-negative reactions for poliomyelitis completing the series, 98% showed a significant response to type 2, 89% to type 1, and 69% to type 3. Response to diphtheria and tetanus was excellent, with 100% showing protective levels of antitoxin. Only 61 postimmunization serums were available for testing for pertussis agglutinin; of these, 76% showed a titer of 1:50 or greater, a significant response considering the relatively low potency of the pertussis component. Children with preimmunization antibodies responded to the heterologous antigens in Quadrigen as well as did those without, suggesting that the "crowding-out" phenomenon [14] was not a problem in this study of combined antigens.

Since the effectiveness of the combination of diphtheria, tetanus, and pertussis is well documented in this age group, only poliomyelitis antigen response is detailed. Figure 3 illustrates that older children respond much more dramatically than do the infants. A definite response, nevertheless, is demonstrated in the 4-to-6-month group.

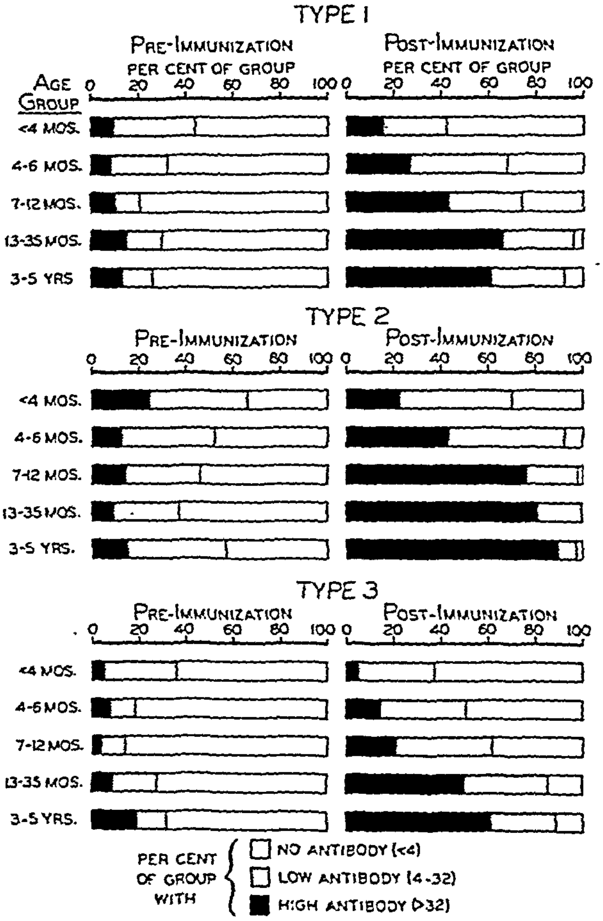

Fig. 3.—Change in poliovirus neutralizing antibody distribution in 224 children one month after three inoculations of Quadrigen given one month apart.

The low response in the 2½-month-old and 3-month-old infants is more apparent than real since there is a three-month interval between the two bleedings charted, and a marked decline in demonstrable antibody status would normally occur in this age group due to the progressive loss of material antibody. Therefore, the fact that antibody status is relatively unchanged is probably indicative of a vaccination response.

As has been noted, the plan of the study included a fourth inoculation for all children under 6 months of age, and the response of 46 infants one month after this fourth dose is shown in part *A* of figure 4. This final dose of antigen was quite effective, since for each serologic type approximately 80% exhibited significant levels of antibody as compared to the lower response to three doses. To show that this result was influenced by the three previous inoculations, the distribution of antibodies among a comparable group of 43 nonimmunized children in the same age range prior to and one month after their first inoculation has been charted in part *B* of figure 4. In this case there was no significant response to types 1 and 3 and only slight change to type 2. Not only do these data, illustrating the "priming" effect of the initial inoculations, support the above conclusion that 2-month-old and 3-month-old infants did respond, but they justify the recommendation of a fourth dose in this age group.

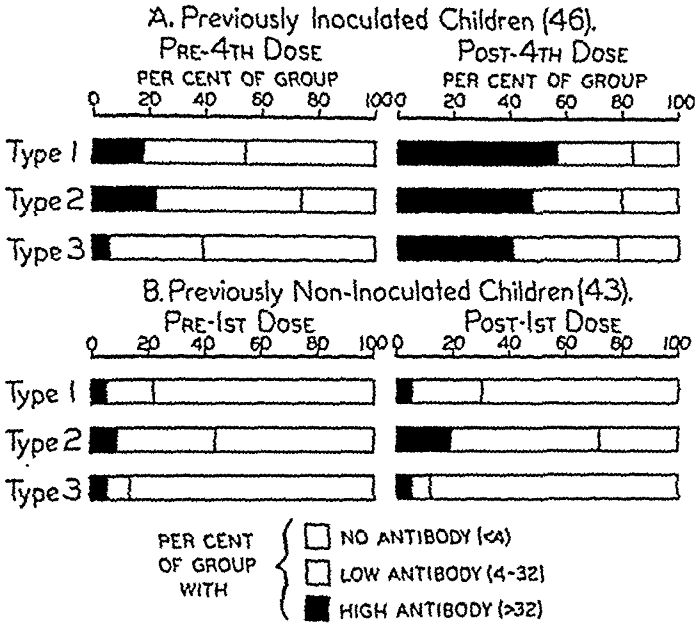

Fig. 4.—Poliovirus antibody resulting from one dose of Quadrigen in previously inoculated and noninoculated 5-month-old to 7-month-old children.

A significant number of the children from this study are currently receiving a stimulating dose of Quadrigen 15 to 16 months after their primary series of inoculations. Antibody evaluation studies of this booster will be part of a more complete report at a later date.

Summary

A practical multiple-antigen poliomyelitis vaccine containing diphtheria, pertussis, and tetanus antigens (Quadrigen) has been prepared, and its effects have been studied in a group of children ranging from 2½ months to 5 years of age.

Incidence of preimmunization antibodies in the studied group was lowest in the 7-to-9-month age group, indicating a need for active immunization prior to this age. Good antibody response was obtained to all antigen components of Quadrigen in children from 2½ months to 5 years of age. A fourth dose was found to be desirable for children less than 4 months of age to enhance poliovirus antibody levels.

Joseph Campau Avenue at River (32) (Dr. Carnes).

Professional assistance in obtaining blood specimens was furnished by the resident medical staff of the Children's Hospital of Michigan through Paul V. Wolley Jr., M.D., Pediatrician in Chief. Technical assistance in evaluating these serums was provided by the virus research testing group at the Parke, Davis and Company Laboratories.

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* * *

NEW PLEURAL BIOPSY NEEDLE

PRELIMINARY STUDY

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e pleura[1] was first used after it was shown by Small[2] and others[3] that open biopsy of the pleura was often a good indicator of underlying pulmonary disease. In expert hands the use of the Vim-Silverman needle has produced some very gratifying results. It has, however, two disadvantages: 1. A pleural specimen is often not obtained. 2. There is a danger of boring out a core of lung, especially when there is only a very thin cushion of pleural fluid.

In an attempt to overcome these difficulties, I have designed an instrument. Its most important unit is a curet-like needle, which has a side slot shaped as in figure 1 *C* and is set 2 to 3 mm. from the terminal blunt end; the blunt tip is closed except for a small central hole which allows, if necessary, a small needle to push out the tissue specimen. The needle stop fulfills the purpose of adjusting the size of the "bite" and of orienting the operator to the side on which the slot is located. The curet needle fits very snugly within a shorter cannula (fig. 1 *A*) which has a cutting terminal edge. The length of the slot and, hence, the bite can be varied by setting the needle stop forward for a small bite and backward for a longer cylinder of tissue. The third part of the instrument is a short beveled needle (fig. 1 *B*) which fits in the cannula (fig. 1 *A*) and is utilized to introduce the cannula to the pleural edge.

Procedure

With the patient under local anesthesia, a small nick is made in the skin with a scalpel blade (no. 11), and the cannula and needle are introduced until pleural fluid is obtained. The needle is now withdrawn slightly until gentle syringe suction does not yield any more fluid. At this point the cannula is situated just outside the pleura. The inner needle is removed, and the curet, attached to a 2-cc. syringe, is introduced to the hilt or until fluid is obtained. In order to get a good bite, the instrument is pushed laterally in the direction of the slot; this maneuver will feed pleural and subpleural tissue into the side opening. The curet is now pulled out gently until it is felt to catch the parietal pleura by its hook-like projection. At this point the cannula is advanced with the other hand with a rotating motion until it has cut a small plug of tissue (fig. 1, part 3). Now the instrument can be withdrawn with ease. The needle cuts a specimen measuring approximately 2 mm. × 3 mm. containing pleural and subpleural tissue (fig. 2).

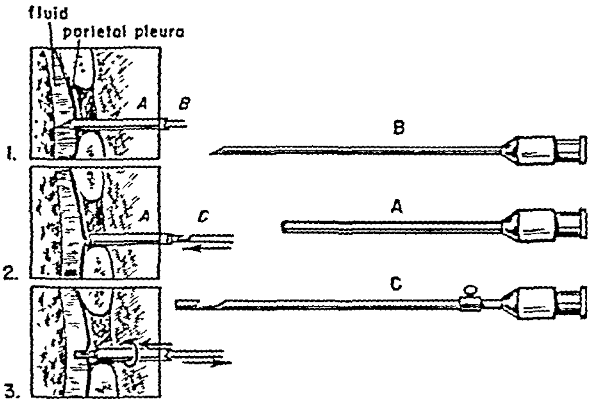

Fig. 1.—*A*, *B*, and *C*, components of biopsy needle. Parts *1*, *2*, and *3*, technique for obtaining pleural tissue.

Comment

This procedure has so far been performed on 10 patients without any morbidity. Another advantage of this instrument is that it is well adapted for use in thoracocentesis because of its blunt end. Thus, it has become my custom to tap all pleural effusions

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with the needle and, just before withdrawing it, to cut a small plug of tissue, thus accomplishing both duties in one operation.

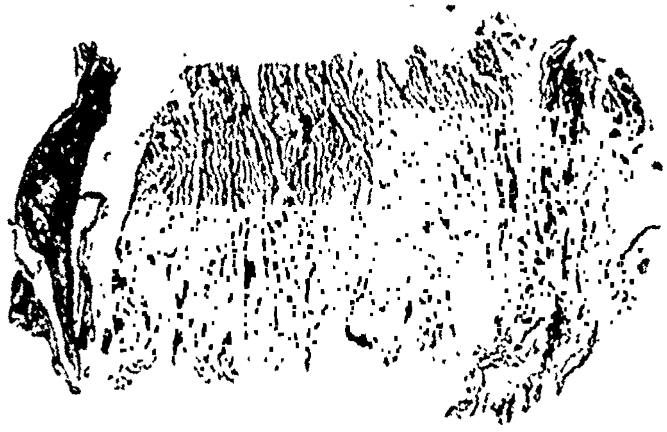

Fig. 2.—Biopsy specimen of pleural and subpleural tissue invaded by tumor cells.

Since the level of the parietal pleura is located by the hook of the curet needle, this instrument is also adapted to taking a biopsy in the absence of fluid without damage to the lung; thus tissue specimens were obtained in three patients where a pleural effusion was suspected but not confirmed on needle aspiration. It is expected that the instrument will be of equal use in peritoneal biopsy, pericardial biopsy, synovial biopsy, and the biopsy of accessible cyst-like structures.

Summary

A new type of pleural biopsy needle has been designed. In a series of 10 patients, it has been found to be safe and reliable.

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CONVENIENT DEVICE FOR VENOUS PRESSURE DETERMINATION

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and
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Though numerous techniques[1] are available for estimation of venous pressure in man, they are all either so cumbersome or so inaccurate that their usefulness is impaired. Among the systems that are widely used, the one of Lyons, Kennedy, and Burwell[1a] is perhaps the most commendable because of its use of an easily reproducible baseline: the level of the back as determined with a spirit level. The rest of their method, however, is relatively elaborate and discouraging. The simplest technique is that of Moritz and von Tabora,[1b] in which a calibrated manometer filled with saline solution is attached to a needle in an arm vein, but its lack of any clearly defined zero reference level diminishes its value considerably. To be most useful, a method for determination of venous pressure should be easy to perform and should give reproducible results with as narrow a normal range as possible. It is the purpose of this paper to describe a technique which has been devised to satisfy these criteria.

Apparatus

The apparatus (see figure) consists basically of a rigid strip of aluminum (*A*) to which is hinged a second piece (*B*), fitted with a catch to hold it vertical. A carpenter's spirit level is attached to the first strip, and there is a centimeter scale on the upright. A sliding, hinged bar (*C*), with a stop at 90 degrees, is attached to one side of the upright and a sliding piece (*D*) with a spring clamp to the other. The whole apparatus can be folded flat when not in use and stored inconspicuously.

The patient lies on the bar (*A*), and the thickness of his chest at the fourth intercostal space is determined by the moving bar (*C*), which then may be folded upwards out of the way. A manometer with a three-way stopcock at its base is attached to the clamp at *D* and adjusted so that the center of the stopcock (0 on the manometer's scale) is at the desired reference level. A syringe containing isotonic sodium chloride solution (0.9 NaCl) is attached to one arm of the stopcock, and a disposable plastic connecting tube leads from the

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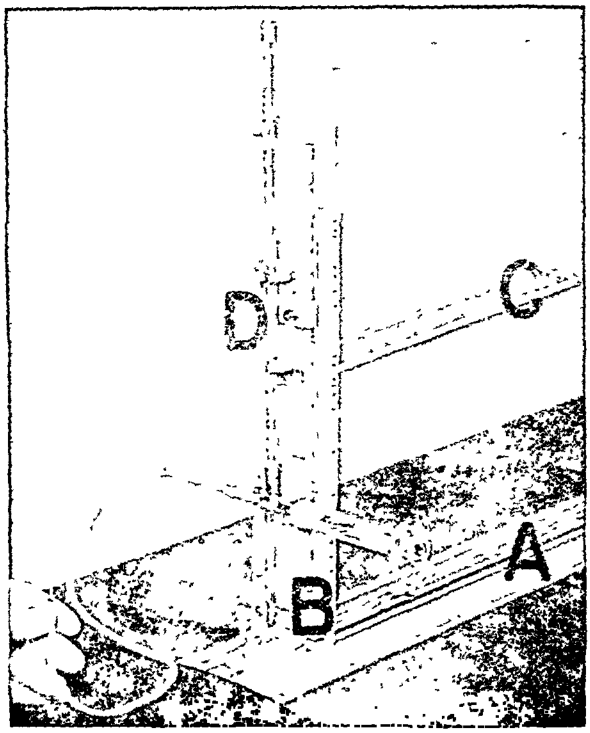
third outlet to a needle. With the system filled with the solution and the apparatus horizontal, as determined by the spirit level, the needle is inserted into an arm vein. Venous pressure is read from the manometer after the stopcock handle has been turned to connect it with the tube leading to the vein. Repeat determinations can be done quickly by flushing and refilling the tube from the syringe reservoir and manipulating the stopcock handle.

For patients with extreme orthopnea, the whole apparatus may be set up while the head of the bed is elevated, and the patient need not be horizontal for more than the short time necessary for the fluid column in the manometer to come to rest.

Comment

The venous pressure, at least for clinical purposes, need be regarded as only a function of the right ventricular end diastolic pressure and not necessarily an absolute measure of it. For this reason, it is more important that the clinician know the range of normal values to be expected with the zero reference level he uses and that the level be clearly defined when the venous pressure is recorded than that any particular technique be insisted on. With the apparatus described here, it is equally easy to refer pressures to a zero level 10 cm. anterior to the back, as proposed by Lyons, Kennedy, and Burwell,[1a] 5 cm. dorsal to the fourth costochondral junction, as used by Friedberg,[2] or any other point of reference. If the posteroanterior diameter of the patient's chest is recorded, as well as the reference level, the value for venous pressure can be "corrected" easily for comparison with data obtained by any method.



Apparatus for determination of venous pressure.

We have chosen to use 60% of the posteroanterior diameter of the chest anterior to the back as the zero reference level. This position was suggested by work of Guyton and Greganti.[3] With allowance for varying thickness of the chest from patient to patient, it makes possible a relatively narrow range for normal values. Fifty patients without clinical evidence of cardiopulmonary disease have been studied with this technique. They were all hospitalized adults, and the posteroanterior diameter of their chests ranged from 14 to 27 cm. The mean normal venous pressure was 79.5 mm. 0.9 NaCl, with a standard deviation of 26.4 mm. and a range of 30 to 181 mm. 0.9 NaCl. Only five readings were less than 50 and three greater than 105 mm. 0.9 NaCl. In these same "normals" the hepatojugular reflux was tested by exerting firm manual pressure over the right upper quadrant of the abdomen for one minute. Response to this varied from a fall of 5 mm. 0.9 NaCl to no change. In no instance was there a rise. In five patients with no cardiopulmonary disease and in whom there was no reason to suspect that the venous pressure should change from day to day, it was found that values obtained over periods ranging up to six days did not vary more than 11 mm. 0.9 NaCl, and usually not more than 6.

Summary

A simple device for easy and accurate direct measurement of systemic venous pressure yielded the following results: Normal values in adults without cardiopulmonary disorder ranged from 30 to 181 mm. of isotonic sodium chloride solution (0.9 NaCl), with only five readings of less than 50 and three greater than 105 mm. 0.9 NaCl. The mean was 79.5 and the standard deviation 26.4. The zero reference level used was 60% of the posteroanterior diameter of the chest at the fourth intercostal space anterior to the back.

This study was supported in part by grants from the Adams County Heart Society and the Mississippi Heart Association.

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DIAGNOSTIC PROBLEMS

REMITTING OBSTRUCTIVE JAUNDICE WITH JACKSONIAN EPILEPSY

Clinical Pathologic Conference (PM 887-54), Jan. 24, 1957, from the Department of Pathology and the Hektoen Institute for Medical Research of Cook County Hospital, Chicago, presented for publication by Daniel S. Kushner, M.D., and Paul B. Szanto, M.D.

Clinical Data

A 50-year-old Negro entered Cook County Hospital "not because he felt ill but at the urging of friends." He admitted to chronic alcoholism, consuming a fifth of whiskey (757 cc.) daily. He had felt well, however, until two weeks previously when he had a chest cold, blood in his stool, anorexia, and loss of 10 lb. One week later, his sclerae turned yellow, his stools became white, and his urine brown. Since then, he had been having chills, fever, and itching of the palms and soles. He denied abdominal pain, fatty food intolerance, or recent parenteral injections.

Physical examination revealed an alert, cooperative, well-developed, and well-nourished man in no distress. His sclerae were intensely icteric. His heart was not enlarged; normal sinus rhythm was present; the aortic second sound was greater in intensity than the pulmonic second; and a soft systolic murmur was present in the mitral area. His liver extended 2 fingerbreadths below the costal margin and was tender. Rectal examination revealed a slightly enlarged prostate, external hemorrhoids, and clay-colored stool; the benzidine test was positive (1+).

Urinalysis revealed albumin 1+; a trace of sugar, bile 4+, and no urobilinogen. His hemoglobin level was 83%. His leukocyte count was 8,100 per cubic millimeter, with 74% polymorphonuclear cells, 12% lymphocytes, 7% monocytes, 5% staff cells, and 2% eosinophils. The platelet count was increased. A blood smear showed 1+ anisocytosis, polychromatophilia, targeting, evidences of toxicity, and 1 Turk cell. Roentgenograms of the chest and abdomen showed only a calcification in the aortic arch. The nonprotein nitrogen level was 27 mg. per 100 ml.

The patient was given a high-protein diet, supplemental vitamins, and 1 Gm. of chlortetracycline daily. He was discharged, condition unchanged, on the fifth hospital day. Two weeks later, he was readmitted, complaining only of generalized itching. Pertinent physical findings again consisted of intense icterus and a somewhat tender liver edge extending 2 fingerbreadths below the costal margin, without splenomegaly. Urinalysis showed a specific gravity of 1.026, albumin and sugar negative, bile 4+, urobilinogen 1+, and formed elements negative. Four subsequent specimens revealed bile (3 to 4+) and no urobilinogen. Much later in the course, bile was 2+, urobilinogen 3+. A preterminal specimen showed a trace of albumin, sugar 4+, and a trace of urobilinogen. The hemoglobin level was 59%.

The erythrocyte count was 3,640,000 per cubic millimeter. The leukocyte count was 13,350 per cubic millimeter, with 70% polymorphonuclear cells, 21% lymphocytes, 4% monocytes, 3% eosinophils, 1% basophils, and 1% staff cells. The platelet count was increased. A blood smear revealed rouleaux formation, anisocytosis 1+, polychromatophilia, targeting, and evidences of toxicity. The prothrombin time was 15 seconds (control 14 seconds). Roentgenograms of the skull revealed no evidence of trauma or sella turcica deformity; calcifications were present in the falx cerebri. Biochemical data are shown in the table. Electrocardiograms were negative.

The patient was treated with penicillin, streptomycin, and intravenous infusions. Clinically, progressive improvement was manifested by decreasing icterus and increasing appetite. A low grade fever of 99 to 100 F (37.2 to 37.8 C) persisted. The stools were brown. On the 54th hospital day, the patient suddenly developed convulsive seizures that began with paresthesias in the right arm, followed by jerking movements of the arm, spreading to the right leg. They occurred several times daily at first, lasted several minutes, and were followed by a short period of sleep. From the 59th hospital day on, the seizures occurred every five to eight minutes, lasting only a minute. Sometimes they began on the left, but more often on the right. Tonic convulsions with carpal spasm and generalized rigidity predominated, but slight clonic convulsions were also described. The patient's state of consciousness varied. At the onset of the convulsions, a neurological examination revealed no abnormalities, but as the seizures became more frequent, dilatation of the pupils and poor reaction to light were observed. The retina showed no abnormalities. The reflexes were hypoactive but bilaterally equal, and no pathological

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reflexes appeared All extremities moved with good strength There was no nuchal rigidity. Sensation was intact.

A lumbar puncture revealed a negative Pandy's test, an initial pressure of 100 mm. H_2O, absence of spinal block, and a leukocyte count of 250 per cubic millimeter An electroencephalogram, made during a seizure, showed spikes of seizure-discharges with stupor waves following. The discharges were generalized, there was no focal accentuation. The patient did not respond to administration of phenobarbital, diphenyhydantoin sodium, or calcium gluconate. He continued to have convulsions Three days before he died, his temperature began to rise, reaching 106 F (41 C) on the day of his death He died on the 63rd hospital day, about three months after the onset of his illness.

Summary of Biochemical Data

Laboratory Values	5/19	5/24	5/25	6/7	6/16	6/25	7/6	7/15	7/19	7/20
Nonprotein nitrogen, mg /100 ml	43	40	53							74
Creatinine, mg /100 ml										3.8
Fasting blood sugar, mg /100 ml										910
Calcium, mg /100 ml									11.2	11.1
Phosphorus, mg /100 ml									5.1	
Total protein, Gm /100 ml	7.2	6.4	6.3	6.4	6.4	6.4		8.3		
Cholesterol, mg /100 ml	207	164	150		240	235	200	197		
Cholesterol esters, %		22								
Alkaline phosphatase Bodansky units	9.7	8.8	9.7	12.1	16.5	17.6	33.5	19.9		
Icteric index, units	221	227	199	176	131	76	49	59		
Cephalin flocculation	0		1+	0	1+	1+	0	0		
Thymol turbidity, units	5.7		3.5	2.8	3.4	2.6	5.7	6.0		
Gamma globulin, Gm /100 ml	1.92		2.02	2.16	2.05	1.89	2.16	2.24		
Sodium, mEq /liter										135
Chloride, mEq /liter										102
Potassium, mEq /liter										5.4
Carbon dioxide combining powers, vol %										22
Cerebrospinal Fluid										
Glucose, mg /100 ml									250	
Protein, mg /100 ml									40	
Chloride, mEq /liter									130	

Clinical Discussion

Dr. Frederick C. Steigmann: With the history of alcoholism, the onset of jaundice following an upper respiratory infection, and the results of the hepatic tests, one may consider that this man had a fatty liver with jaundice due to a so-called toxic hepatitis We frequently see alcoholics who get along well for months and even years until some external factor precipitates jaundice in a previously silent fatty liver. This may be just one more bout of alcoholic excess, an infection, a hemorrhage, or trauma. In this patient, the chest cold provided a source of infection for the precipitation of jaundice in a patient with a fatty liver. The count of 13,000 leukocytes per cubic millimeter might be used in support of the assumption of infection. The liver was enlarged and tender, as the fatty liver often is. Some such patients are even considered to have an acute abdomen. This man had pruritus, which one associates with obstructive jaundice, but cholestasis is not infrequent in a patient with a fatty liver. His initial response to tetracycline was also typical of that seen in the fatty liver syndrome. His chills and fever might have been due either to the infection that precipitated the jaundice or, more likely, to the cholangitis that so frequently accompanies biliary obstruction. The normal flocculation tests in the face of severe icterus are entirely consistent with an active fatty liver syndrome.

Despite these arguments for a fatty liver syndrome in a poorly nourished chronic alcoholic who got an infection and toxic hepatitis, we must also consider the possibility of an extrahepatic biliary obstruction. The pruritus and negative flocculations suggest an extrahepatic obstructive jaundice Weight loss and anorexia can occur with any obstructive jaundice, but especially point toward malignancy. Chills and fever can occur with both benign and malignant common duct obstruction. The fact that the urinary urobilinogen, at first absent, later appeared intermittently suggests a fluctuating or incomplete biliary obstruction.

One of the most common causes of incomplete obstruction is cholelithiasis Stricture is another, but there was no history of operation to suggest stricture, and cholelithiasis is extremely rare in the male Negro. Carcinoma in or near the ampulla of Vater can cause incomplete obstructive jaundice because tumors in this area are of the type that become necrotic and slough, so that intermittently bile may enter the intestinal tract; urobilinogen is formed, and there are intermittent dark and light stools with occult blood. I do not believe we can put too much importance on a 1+ benzidine test and only one stool examination, although previously the patient did note blood in the stool We should ascertain whether the blood came from hemorrhoids or higher in the gastrointestinal tract. Blood in the stool in a jaundiced patient is often considered to result from a hemorrhagic diathesis, but when it is associated with an incomplete biliary obstruction, it points to a carcinoma near the ampulla of Vater.

The negative flocculation tests and normal cholesterol level all fit with a diagnosis of obstructive jaundice. The low cholesterol ester determined late is indicative of liver damage, which occurs with prolonged biliary obstruction. Also any of the hepatic tests may become abnormal if biliary obstruction is associated with sepsis. In this patient, we must consider the possibility of a malignant process around the head of the pancreas and involving the ampulla which caused intermittent jaundice as a result of sloughing of the tumor, permitting blood to enter the intestinal tract. In any patient with prolonged jaundice, one must x-ray the gastrointestinal tract to exclude a gastrointestinal malignancy.

In this case, roentgenograms of the chest and abdomen were negative. The value of a search for opaque stones in KUB films of jaundiced patients is overrated. Even if one sees an opaque shadow, this is not necessarily the cause of the jaundice. The negative roentgenogram of the chest was important because if it had shown pneumonitis, we would have considered that as a possible precipitating cause of the jaundice. The next problem is that the patient appeared to improve. His icterus index was much lower at the time of his death than previously. One ordinarily assumes that this means medical jaundice, and that it is a sign of improvement. In obstructive jaundice, one sees a slow drop in the icterus index, which is usually slight and is considered to be due to a developing secondary anemia. Here the hemoglobin level fell from 83 to 59%. A fall in the icterus index from 200 to 70 cannot be due just to anemia; there must be some other explanation. In a case such as this, as the index improves one would expect the patient to improve clinically and get well, but instead, about two weeks before his death, he suddenly developed tonic and clonic convulsions which in a few days became bilateral and continued until his death, with high fever.

It is possible that the convulsions were related to hepatic coma, but in our experience generalized convulsions are rare in hepatic coma. Moreover, this patient was conscious at the onset of his seizures. Davidson[1] states he meets this combination rarely, but Adams and Foley[2] have emphasized the association. It is possible that this man had hepatic coma. Unfortunately, I cannot interpret the electroencephalographic findings. Electroencephalograms in hepatic coma (Foley) show "paroxysms of bilaterally synchronous symmetrical high voltage slow waves in the delta region." That does not fit with the description given here. The cerebrospinal fluid contained 250 cells. It is unusual to have a negative Pandy's test with so many cells present. Another possibility is that the convulsions were the result of cerebral metastases from a malignancy of the biliary tract, especially since the seizures began focally. We must also consider the possibility of a cholangiolitic hepatitis due to any one of many drugs. I have not, however, seen convulsions following this condition. These cases are usually protracted and may terminate in hepatic coma, but this patient seemed to improve before he became comatose.

Although there is no mention of abdominal pain, which he might have had with a biliary tract neoplasm, I believe that this man probably had a neoplastic lesion in the biliary tract near the ampulla of Vater, with an incomplete obstructive jaundice. This may have given him a cerebral metastasis. I would not, on the other hand, be amazed if he had a fatty liver syndrome terminating in hepatic coma.

Dr. William Meszaros: The roentgenograms were mostly negative. The skull was normal and the sella turcica not enlarged. The anteroposterior view of the skull was normal except for calcification in the falx, which is not significant. The flat plate of the abdomen showed no abnormalities. The liver and spleen shadows could not be seen. There were no calcifications in the pancreatic region. The posteroanterior view of the chest showed arteriosclerosis. The heart size was normal and the lung fields clear. All we could demonstrate radiographically was arteriosclerosis.

Dr. Paul B. Szanto: The electroencephalographic tracings showed slow waves which are supposed to be characteristic for epilepsy.

Dr. Steigmann: The electroencephalogram did not suggest hepatic coma.

Dr. S. Howard Armstrong Jr.: I would like to discuss the neurological aspect of this case. Dr. Steigmann suggested a focal cerebral lesion such as a metastasis. There were 250 unspecified leukocytes in the spinal fluid, which can occur not only with tumor or abscess but also with subdural hematoma. Although convulsions are much more common in hepatic coma, subdural hematoma is a possibility.

Dr. Steigmann: That is an excellent suggestion. Very often an alcoholic will come into the hospital with no history of injury or violence, despite the presence of bruises. This patient could have been hit or could have fallen down and sustained a subdural hematoma.

Dr. Szanto: What about the high blood sugar level before death? It went to 910 mg. per 100 ml.

Dr. Steigmann: Also, at first, he had a trace of sugar in the urine. He might have had a pancreatic lesion with a diabetic tendency. Patients with carcinoma of the body of the pancreas may have an abnormal glucose tolerance before the appearance of jaundice.

Clinical Diagnosis.—The clinical diagnosis was biliary tract neoplasm near the ampulla of Vater causing incomplete obstructive jaundice; carcinoma of pancreas with pancreatic diabetes; and focal cerebral lesion due to metastases or subdural hematoma.

Pathologist's Report

Dr. Szanto: The body was that of a well-developed, poorly nourished man with jaundiced sclerae. Both lungs together weighed 1,300 Gm. There was a marginal emphysema and the bronchi contained purulent material. Microscopically, the bronchioles contained numerous leukocytes, the picture of severe bronchitis and bronchiolitis. Horseshoe kidneys were present (350 Gm.), with a superimposed biliary nephrosis. The liver was enlarged (1,800 Gm.). The surface was smooth and the inferior margin was rounded. On section the lobular architecture was preserved and the parenchyma was green. The gallbladder was moderately distended and the cystic duct was dilated. The portal lymph nodes were enlarged and relatively firm. The hepatic and common ducts were dilated, up to 2.5 cm. in circumference. Just before its entrance into the duodenum, the common duct was compressed. The papilla of Vater was normal. The head of the pancreas was firm and nodular, and, on section, of pale gray color with loss of the normal lobular pattern. The pancreatic duct was dilated in its entire length (fig. 1), as is so typical of carcinoma of the head of the pancreas. Microscopically, the portal fields of the liver were enlarged, with evidence of portal and perilobular fibrosis. The liver cells and the liver cell plates were well preserved. Bile casts were seen in the bile capillaries and ductules, with occasional bile extravasates.

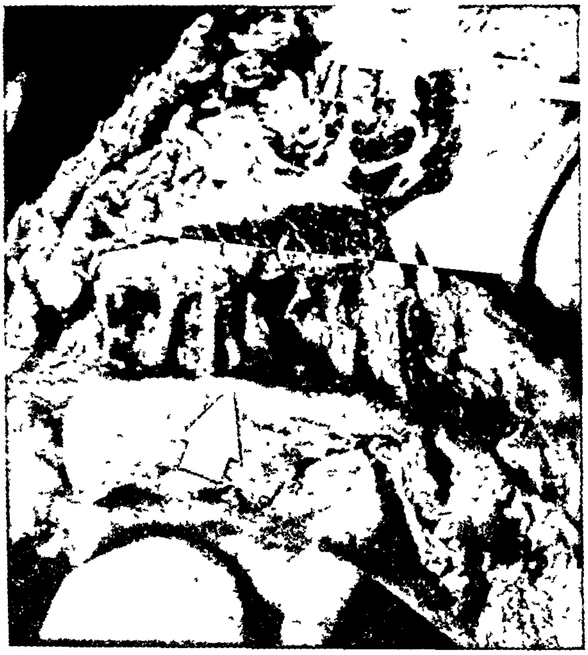

Fig. 1.—Extreme dilatation of pancreatic duct in its entire length.

Examination of large sections taken from the head of the pancreas revealed numerous ductular structures lined by high columnar epithelium. In one area adjacent to the pancreatic duct, the pancreatic parenchyma was completely replaced by tumor tissue, consisting of pleomorphic gland-like structures. The malignant character of this tissue was also evidenced by invasion of the perineural lymphatics (fig. 2). The obstructive jaundice was therefore secondary to an adenocarcinoma of the head of the pancreas. How can we explain the remission of the jaundice? Such a remission may occur if the obstruction is due to a carcinoma of the papilla of Vater or of the common duct proper since, at these locations, the sloughing of the necrotic tumor tissue may alleviate the biliary obstruction. Rarely, even extensive necrosis of a carcinoma of the head of the pancreas has been associated with remission of obstructive jaundice. However, in this case, no necrosis of the tumor tissue was found.

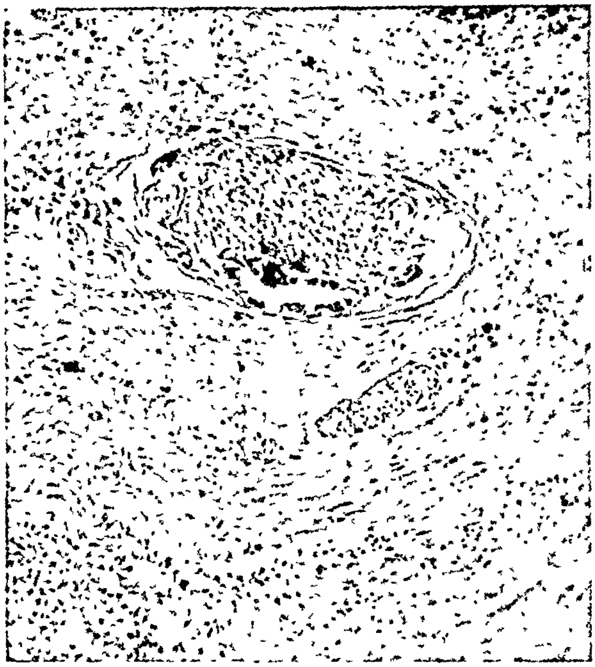

Fig. 2.—Tumor invading perineural lymphatics (hematoxylin-eosin stain, × 80)

Further study of the head of the pancreas around the tumor tissue revealed proliferating ductules with infiltration of connective tissue by inflammatory cells, merging imperceptibly with the carcinoma proper. Sections taken from the body and tail of the pancreas showed interlobular and intralobular fibrosis, lymphocytic and histiocytic infiltration (fig. 3), and marked dilatation of the ductular structures. Some of the islands of Langerhans were hyperplastic.

There is no question that the uniform cylindrical dilatation of the main pancreatic duct is characteristic of obstruction of this duct due to carcinoma originating in the head of the pancreas,[3] and, therefore, the severe pancreatic fibrosis could be explained solely on that basis. Still it seems to us that the changes in the vicinity of the carcinoma, such as fibrosis, ductular proliferation, and inflammatory sweat. Many, if not all, of the purchasable antiperspirant aluminum salt preparations today contain a wetting agent.

Considering the tremendous number of daily applications of aluminum salt antiperspirants to the axillas, the incidence of untoward side-effects is relatively rare. In addition to occasional micropapular dermatoses (similar to prickly heat) and the more deep-seated folliculopapular skin eruptions, there are occasional direct irritant effects and the very rare cases of allergic eczematous contact dermatitis. The tendency to develop folliculopapular eruptions is an individual matter.[11] The individual predisposition, however, seems to occur not only as a sporadic incident but also as a familial trait, for of a total of about a dozen subjects in whom we observed folliculopapular eruptions from antiperspirants, three were siblings of one family, two of another, and two of a third family.

The mechanism of action underlying the reduction of eccrine sweat delivery by aluminum salts is not yet entirely clear. It appears to result from a combination of factors, important among which are a mild inflammatory reaction with edema, expansion of the horny layer at the ductal orifices, and consequent narrowing of the pores.

Among a few less effective agents studied, a simple powder mixture of 3% salicylic acid and 97% talcum produced some reduction of axillary sweating.[2c] Exchange resins also showed a mild antiperspirant effect.[12] This effect was distinctly weaker with anion exchange resins than with cation exchange resins.

More recently, zirconium salts have been incorporated in several antiperspirant preparations. Certain, not altogether rare, papular axillary eruptions of a new type, microscopically resembling tuberculoid granulomas, beryllium granulomas, or silicon granulomas, were attributed to the sodium zirconium lactate which was present in some of the newer stick preparations.[13] Saunders suggests that these granulomas are caused by apocrine duct rupture.[14] Shelley and Hurley, however, recently demonstrated the formation of epithelioid cell granuloma as a result of specific allergic sensitization to zirconium salts.[15]

Causes of Osmidrosis

It is difficult to characterize a body odor as agreeable or disagreeable, since in the domain of olfactory impressions one man's meat is certainly another man's poison—what is attractive or indifferent to one nose is disgusting to another, what is perceptible to one sniffer cannot be detected by another. Nevertheless, certain odors are almost unexceptionally disagreeable to the human olfactory sense. Unpleasant body odors, as a rule, are due to a combination of factors, including changes in the composition of sebum, of keratin, and of the sweat. Microbial activity may well be the major factor responsible for widespread decomposition of each of these three substrates. Malodorous sweating is termed bromhidrosis or osmidrosis.

Generalized bromhidrosis may occur in certain metabolic or infectious diseases.[16] Moreover, certain drugs and even foods may render the sweat odorous, notably valerian, asafetida, garlic, and onions.[16] In a limited number of tests, we have not been able to show that such odors are significantly reduced by the intake of chlorophyllin.

As shown by Shelley and others,[3] apocrine sweat decomposed by microbial activity is the main offender in localized bromhidrosis of the axillary areas. The same investigators emphasized the absence of odor in native apocrine sweat, since they did not detect any odor in freshly produced apocrine sweat in the disinfected axillas of their subjects.[3] Although these observations, by and large, agree with those of Killian and Panzarella,[17] the question of the natural occurrence of odorous substances in "sterile" apocrine sweat appears to require further exploration.

By means of paper chromatography Nitta and Ikai [18] demonstrated that, of the lower unsaturated fatty acids, those with four or more carbons were present in greater quantity in persons with axillary osmidrosis than in persons without osmidrosis. These observers attribute axillary osmidrosis to the combined function of a relatively large amount of apocrine sweat plus its original composition and the action of enzymes, which emanate from microorganisms and alter the composition of the sweat toward formation of the unsaturated fatty acids with four or more carbons.

Whatever may be one's stand on the absolute lack of odor of native apocrine sweat, it is certain that effective deodorants include those which interfere with the growth of bacteria on the skin and in the hair follicles. The aluminum salts show antibacterial activity,[19] and even shaving considerably reduces the axillary odor,[3] presumably because the hairs favor the settlement of bacteria. In addition, the hairs are sites of adherence of odor-producing material. Externally applied antibiotics have proved distinctly effective in controlling axillary odor.[20] Moreover, soaps containing hexachlorophene, which is known to every layman today, or soaps containing tetramethylthiuram disulfide (TMTD) produce a deodorant effect in the axillas for many hours in most persons.[21]

Another category of agents of some promise is that of the exchange resins, as reported by Thurmon and Ottenstein [22] and by Ikai.[23] In agreement with Ottenstein's results in vitro, we obtained a distinct decrease in the pH of the axillary skin by means of cation exchange resins.

Conclusions

In conclusion, it may be stated that the problem of how aluminum salts reduce axillary odor still merits further experimentation; it is possible that these salts may diminish also the outpouring of apocrine sweat. Our microscopic findings [11] indicate that single applications of aluminum salt preparations to the axillas produce changes which have much in common with the features of apocrine sweat retention obtained subsequently by Hurley and Shelley upon massive experimental obstruction of the apocrine ductal orifices with concentrated nitric acid or by electrodesiccation.[24] The common features include dilatation of the apocrine tubules, compression atrophy of the epithelium, and cellular casts in the tubular lumens. In their aggregate, the findings suggest that the mechanisms by which the aluminum salts (and perhaps also certain other deodorant preparations) act in the control of axillary odor may, in addition to the reduction of microbial activity, include a reduction in the actual amount of apocrine discharge to the skin surface.

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COMMITTEE ON MEDICOLEGAL PROBLEMS

FOLLOW-UP STUDY OF FATAL PENICILLIN REACTIONS

SPECIAL REPORT

Abraham Rosenthal, M.D., New York

During the years 1952 and 1953, the Office of Chief Medical Examiner of the City of New York investigated eight fatal reactions after penicillin injection, and I published a report in the *New York State Journal of Medicine* of May 15, 1954, entitled "Eight Fatal Anaphylactic Reactions to Penicillin."[1] This article was immediately widely reported in the lay press in many lands and languages. In the Sept. 4, 1954, issue of THE JOURNAL there appeared a full abstract of the article. In the November, 1954, issue of *Coronet* magazine, a lay science writer abstracted the original article without our knowledge and called it "Penicillin Turns Killer."

From the time of the publication of the original article, a large amount of mail was received both from the medical profession and from the allied professions and laity. All the above is mentioned because by the time the stir this article created wore off, it was hoped that we would have less occasion to encounter fatal penicillin reactions.[2] However, the reason for this report is that, although for a while it seemed that the desired effect of the 1954 publication was being achieved, it has turned out that instances of fatal reactions to penicillin are still occurring.[3] We have in the Office of Chief Medical Examiner of the City of New York for the years 1954, 1955, and 1956 accumulated 18 more deaths. The figures for 1957 are not complete, but we know of at least 4 more, thus making a total of 22 since our last report and, with those published, a total of 30 fatal reactions from penicillin in less than five years.

One readily concedes that in a city like New York, with a population of over 8 million people, there must be countless doses of penicillin administered and that these deaths comprise an infinitesimal figure in the over-all use and unquestioned usefulness of this drug.[4] However, without denying the fact that our population would be far smaller were it not for the almost miraculous good wrought by penicillin, it cannot be overlooked that in many instances an overwhelming reaction to penicillin is preventable.

Since this report is in the nature of a follow-up to the previous publication, it might be of interest to comment on some changes in our thinking since then. It was stated, in 1954, that "no parenteral use of penicillin should be undertaken without first having ascertained the history of previous sensitivity," or that of any type of allergy. At that time it was considered safe to offer the drug by mouth when there was doubt about the possibility of a reaction by its parenteral use. This idea must be changed because now there are reports of fatal and near-fatal reactions not only from orally administered penicillin but even from sucking on a lozenge containing only 20,000 units.[5] Recently there appeared a report from an Army medical installation in Occupied West Germany[6] on the use of a 15-minute intradermal and/or conjunctival aqueous penicillin test, with use of the solution to be given to the patient in the absence of any reaction. There were no fatal reactions. This technique is practical under conditions comparable to an Army hospital, but it is hard to picture the busy general practitioner on his rounds of house calls skin-testing every squirming youngster when in doubt. That it can be done there is no question, but one must be practical. In a busy office, however, it would seem simple enough to make up a fresh vial of 300,000 units of aqueous penicillin daily and to use it for intradermal or conjunctival testing, with a control skin test with the diluent.

But even this method has its pitfalls, for two months after the publication of the article, there appeared a report in the form of a letter to the editor of the *New England Journal of Medicine* from a physician who, in using the conjunctival test, as described in the Army report, had a near-fatal reaction in his office.[7]

Since 1954 the literature has become filled with reports of the discovery and clinical use of numerous new antibiotics, some of which have an unusually wide spectrum of applicability. Although penicillin is the least toxic, is bactericidal, and is about the least expensive of all antibiotics, we nevertheless have a choice of any one of many, such as erythromycin; carbomycin; novobiocin; streptomycin and dihydrostreptomycin; the tetracyclines, that is, tetracycline, chlortetracycline, oxytetracycline; chloramphenicol; bacitracin; neomycin; polymyxin B; viomycin; cycloserine; tyrothricin (for local use); and ristocetin (specifically against staphylococcic infection, this organism being the plague of our modern antibioticized exist-

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ence, especially in hospitals). It should be kept in mind, however, that, of the reactions caused by 809 preparations reported in December, 1957, by the Food and Drug Administration, 793 were caused by penicillin, with 72 deaths, and 16 reactions were caused by streptomycin, dihydrostreptomycin, chloramphenicol, and tetracycline, with 2 deaths.[4]

It is not the province or purpose of this presentation to discuss advances in treatment with antibiotics. One should not under any circumstances abandon the use of penicillin, a drug to which countless numbers owe their lives despite a few tragic mishaps, but greater care must be exercised in its use so that its lifesaving work may go on unimpeded. When there is any question about whether a patient is sensitive to the drug or where there is a history of allergy, as there may well be in one out of seven people,[8] one might consider using another antibiotic in its place unless bacteriological studies and in vitro sensitivity tests indicate penicillin to be the only drug capable of affecting a given organism. In such an instance, there have been developed techniques of desensitization which, although time-consuming and meticulous, have applicability.[9] The patient has to shoulder some of the responsibility for these mishaps. How often does he say to the physician, "Just give me a shot of penicillin and I'll be OK"? However, the physician must be the sole and final judge as to what medication is needed.

Statistical Survey

For statistical purposes, we have included in our present study the 8 cases originally published, thus making the total number of cases 30. In a general way, the following facts may be gleaned as to age, sex, and race. The youngest was one month old, the oldest 66 years old, and the average age 33.8 years. There were 14 males and 16 females. There were 17 white people and 13 Negro. Three persons were 0 to 2 years old; one was in the 2-to-10 year category; none were aged 11-20; 4, 21-30; 16, 31-40; 3, 41-50; 1, 51-60; and 2 were aged 61-70.

Place of Occurrence.—Six deaths occurred in the home, 12 at physicians' offices; 2 patients reacted at home and died at the time of arrival or soon after arrival at the hospital, and 3 reacted at physicians' offices and died shortly thereafter at the hospital. Seven deaths occurred at hospitals, these deaths being subdivided as follows: two patients were hospital employees treated at the employees' clinic, two died in an emergency room, one was a nurse treated by another nurse at the victim's request, and two were hospital patients (one of these being treated for a plantar ulcer in a case of peripheral vascular disease, the other receiving prophylactic therapy after an intranasal operation).

Time of Occurrence.—Twenty-five cases were of the immediate type, and five patients suffered delayed reactions. The time of the delayed reaction was 30 minutes for two patients, 20 minutes for one patient, 2 hours for one patient, and 14 days for one.

Dosage.—The amount of penicillin used was anywhere from 200,000 to 500,000 units. In two instances 20 mg. of chlorpheniramine (Chlor-Trimeton) maleate was administered in the injections; in one case 2 cc. (equivalent to 10 mg.) of a diphenhydramine (Benadryl) hydrochloride ampul was given simultaneously. These last three cases are the result of the warnings given by the drug houses, namely, that it is less risky, when there is doubt, to use simultaneously a dose of an antihistamine. This advice could have been misleading, since when protection against anaphylaxis is needed, the action of the simultaneously administered antihistamines could never be fast enough to save life. That the antihistamines might minimize a less catastrophic reaction might very well be, but they probably never prevented a death. Within the past few months a penicillinase preparation[10] has been made available which can be administered when a reaction is noted to be beginning, but even here the manufacturer admits its limitations in the type of event which occurred in 25 of the 30 cases. It is recommended by the manufacturer that this preparation be kept as handy as epinephrine and that it may even be used intravenously followed by another dose (800,000 units per dose) given intramuscularly almost simultaneously. The manufacturer should be complimented for being very clear in his instructions since he does state: "NOTE: In the rare acute anaphylactic reactions that cause patients to expire in minutes Neutrapen would not have time to be effective."

History.—In 14 cases no inquiry at all was made as to prior administration of and/or reaction to penicillin. In three cases the patients exhibited asthmatic symptoms which should have put the physician on guard in the use of penicillin, since reactions may be more apt to occur to penicillin in patients with a history of asthma. In only one instance do we have complete authenticated evidence of a direct inquiry having been made and a negative answer obtained. With reference to three persons known to have reacted previously, the physicians stated that they had made inquiry and received negative replies but the reverse was alleged by the patients' families. In only 7 cases are we absolutely certain of a prior known sensitivity, and in 12 cases we could not obtain an authenticated history of a prior reaction. From all this it is obvious that one is hard pressed in making a survey of this type to get the crucial information because of the subsequent possibility of a legal problem.

Indications for Use of Penicillin.—The part of the study concerning indications for the use of penicillin necessarily requires sincere objectivity, albeit there was arbitrariness on our part. Thus, the cases have been divided into 12 in which it is felt the use of penicillin was indicated (omitting for the moment the matter of inquiry about previous use and reaction or lack of it), 13 cases in which the indication for the use of the drug was questionable, and 5 cases in which we thought it was not indicated. The diagnoses for which the drug was given are enumerated and have been arbitrarily divided as to indications as follows: The use of the drug was indicated for upper respiratory infection with fever in 4 patients; for venereal disease in 5; for erysipelas in 1; for peridental abscess in 1; and for plantar ulcer in 1; for a total of 12. Indications for use of the drug were questionable for upper respiratory infection without fever in 12 and for paronychia in 1, for a total of 13. The drug was not indicated for nonspecific skin eruption in one, for sprained toe in one, for injury to a finger in one, for stasis dermatitis in one, and for postoperative intranasal surgery in one, for a total of five.

Legal Aspects

Nine cases of fatal reaction to penicillin are or have been the subject of lawsuits as far as we can determine from our files. On this latter point a careful search was made of the New York County Lawyers Association Library. Inquiry was also made of the National Association of Claimant's Compensation Attorneys executive office and from a few prominent New York attorneys, even those associated with the malpractice claims against the doctors of New York State, about their knowledge of any court rulings on any similar cases. None recalled any. However, it is not unlikely that whatever claims were made either were settled just before they reached court or, having been tried, were not appealed. We know of one instance where the physician made a cash settlement because he did not carry malpractice insurance.

In going over the legal aspects of this problem, the following paragraph in Warren's "Negligence in the New York Courts" was noted: [11]

> To a large extent, at least, the knowledge and skill required of a physician or surgeon depends upon the state of the profession. . . . he is required to have the knowledge and skill of the average member of his profession in good standing in the community in which he is practicing. This means, of course, that he is not required to anticipate future discoveries. It is an elementary proposition that the medical profession advances in knowledge as time goes on. New discoveries are constantly being made. As a result of this, at the time of a trial of an action such new discoveries may have rendered improper a course of treatment previously followed. If, however, this treatment, at the time it was given, followed that generally used by members of the medical profession at that time, it will free the physician from liability.

The above paragraph is self-explanatory. Insofar as the penicillin problem is concerned, there is no longer any doubt as to the ability of this drug to cause fatal reactions, nor can it be denied that by now such possibility should be known to all who use it.

But even the greatest care in inquiring about any previous use of penicillin and/or reactions thereto may fail to reveal unknown sensitization. Two facts have shed some light on the possible means of such sensitization. One concerns the innocent ingestion of penicillin through the drinking of milk, and the second concerns penicillin formation and its absorption from skin where it was made by pathogenic fungi. As to the milk problem, reports in *Veterinary Medicine* [12] state that 5.9% to 11.6% of the milk reaching the consumer contains penicillin in concentrations ranging from 2 to 80 units per glass.[13] The penicillin had been injected by the farmer into the cow's udder for the control of mastitis, which cleared in a day or so, making that cow's milk marketable, but it takes about four days before all the penicillin disappears from the udder. Warnings on labels not to market the milk for at least 72 hours are often completely disregarded. Thus, the patient may unknowingly become sensitized to penicillin. The second means of unsuspected sensitization was shown many years ago by Peck and Hewitt [14] and recently by some Hungarian investigators who noted that pathogenic fungi living on the human skin could, in some instances, produce penicillin. The latter could then be absorbed and in time sensitize the individual to penicillin and thus be the basis for a later reaction to the drug when used therapeutically.

Therefore, it is now apparent that the physician is faced with a true dilemma, since even the most careful and complete questioning of a patient may give him no warning about a subsequent reaction. Most people drink milk, and not a few have or have had some form of epidermophytosis. It seems reasonable, in the light of the above work, to avoid the use of penicillin in people with a history of "athlete's foot." In order to illustrate more vividly the problem of fatal penicillin reactions, a few selected cases are described.

Report of Cases

CASE 1.—A 38-year-old female was under treatment by her physician for syphilis. She had had two prior injections of penicillin, of 600,000 units each, the last one about a month before the present one. At this visit, the physician stated to the medical examiner that he had made an inquiry about any previous reaction and had received a negative reply. He then injected 600,000 units of procaine penicillin intramuscularly into the buttock. Within a few moments the patient complained of feeling dizzy, collapsed, and, despite the injections of epinephrine and coramine, she died. While the details of the story were being obtained from the doctor at his office, the scene of the death, the patient's husband appeared, having been notified of the death by the physician and the police. The husband was questioned about his wife and it was learned from him that after the previous injection about a month before, his wife had developed "bumps" all over her body and was sick for about 12 days thereafter. He further stated that they had called the physician to notify him of this occurrence. The doctor denied any knowledge of this information. The vial from which the drug was drawn was checked by our chemists and identified as procaine penicillin and was not outdated. A complete autopsy was performed, and other than old tuberculous peritonitis, nothing was found but visceral congestion. The injection site revealed that the penicillin crystals had not entered any blood vessel. Microscopy was negative except for visceral congestion and tuberculous peritonitis.

Case 2.—A 40-year-old female was being treated at her physician's office for a "sprained toe." She was given 300,000 units of procaine penicillin intramuscularly, and, while receiving some physiotherapy to her toe, she began to feel weak, complained of respiratory distress, collapsed, and was pronounced dead about a half hour later despite the use of stimulants. Inquiry by the medical examiner of the doctor as to any previous reaction yielded a negative answer. However, the husband of the deceased told the medical examiner that about three months before his wife had had a "bad reaction" after an injection of penicillin for a "sore throat." A complete autopsy was entirely negative. Even a dissection of the "sprained toe" failed to reveal any local tissue changes. Microscopy was negative except for visceral congestion.

Case 3.—A 33-year-old female was seen at her physician's office for the treatment of a paronychia of the left thumb. The doctor stated that he had made inquiry of the patient about previous use of penicillin and learned that she had received penicillin before but had not had any untoward reaction after its use. He then administered 300,000 units of procaine penicillin intramuscularly. The patient left the office but returned a few minutes later stating that she was not feeling well, and she was noted to be in respiratory distress. The doctor placed her on the waiting room floor, gave her an injection of epinephrine, and called for an ambulance. She was admitted to the hospital in coma and died about an hour later despite all measures taken to revive her. Dr. Helpern performed this autopsy and reported pulmonary congestion, some laryngeal edema with encroachment on the aperture of the larynx, abundant viscid mucoid secretions in the trachea, and a paronychia on the radial side of the left thumb.

Case 4.—A 31-year-old male reported to his physician's office, complaining of a sore throat. The doctor examined him and found that the patient had a "red throat" and fever. The physician suggested that the patient be hospitalized, but this was refused. The patient was then given 600,000 units of procaine penicillin intramuscularly. The patient went home and prepared for bed while his wife went out to fill a prescription. Upon her return, he was dead. The medical examiner investigating the case was told by the physician that inquiry had been made about prior penicillin administration to which an affirmative answer was obtained and that the patient had made no mention of any reaction to the drug. However, the patient's wife told the medical examiner that about a year before this he had received penicillin for some minor ailment after which he had angioneurotic edema. A complete autopsy revealed pulmonary edema and congestion and some laryngeal edema.

In all the above cases complete chemical examinations of the viscera were made by the toxicological laboratory of the Office of Chief Medical Examiner with negative findings. Microscopically only intense visceral congestion was noted except where pneumonitis was found and in those cases it was postulated ante mortem.

Summary

A statistical survey of 30 authenticated fatal anaphylactic reactions to penicillin, recorded in the files of the Office of Chief Medical Examiner of the City of New York, has many implications. There is the possibility of unknown sensitization to penicillin by means of the ingestion of penicillin-containing milk and its products or by absorption through the skin from dermatophytes, thus paving the way for a later unpredictable reaction to the therapeutic use of the drug. Careful inquiry regarding the patient's allergic reactions in the past should precede the administration of penicillin. Such safety measures are important for their legal implications as well as for the sake of the patients.

The author wishes to express his appreciation to Dr. Milton Helpern and the entire Medical Examiner Staff for their kind assistance in the preparation of this material.

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PERINATAL MORTALITY AND MORBIDITY PROGRAMS IN THE UNITED STATES

THE PROBLEMS *of perinatal mortality* and morbidity are currently more prominent than those of maternal mortality. The latter have been attacked vigorously for some time, and where this has been done the lowering of maternal mortality rates has, on the whole, reduced perinatal deaths as well. In other words, good maternal health is associated with healthy newborn infants. Nevertheless, these efforts have not been enough. The large number of early infant (neonatal) deaths has long deterred many committees and medical study groups from attempting any sort of comprehensive mortality analysis such as has become relatively common for maternal deaths. The time has come, however, when more concerted effort must be directed toward problems more specifically related to the reduction of perinatal mortality and morbidity.

Recent national statistics show a continuous and significant decrease in maternal deaths, whereas the rate of decrease of neonatal deaths is proportionately much less. This is in spite of the fact that the "irreducible minimum" in maternal mortality was thought by some to have been reached several years ago. The maternal mortality rate for 1956 was 3.8 deaths per 10,000 live births, as estimated by the national office of Vital Statistics.[1] This is a 76% reduction during the 10 years since 1946. In contrast to this is the relatively low reduction in neonatal deaths, only 22% during the same period. The total number of infant deaths registered in the United States in 1956 was 108,300 (26 per 1,000 live births), of which 78,160 (72%) were during the first 28 days (the neonatal period).

"Perinatal" is a relatively new term already widely used by many workers in this field. In many instances it is used to include neonatal deaths and late and intermediate fetal deaths. However, inclusions used in calculating the perinatal mortality rate vary from one place to another with respect to the maximum length of time after birth and the minimum number of weeks of gestation. The number of fetal deaths reported approximates that of neonatal deaths, but because of the varying degrees of completeness in the reporting of fetal deaths, the total number is not accurately known. For this reason rates are often based upon total live births rather than total births.

The Committee on Maternal and Child Care is studying these problems of the perinatal period (neonatal and fetal) and the current efforts to solve them. In cooperation with other interested persons and groups, the Committee is working toward the development of a study guide on this subject for state and local medical societies, health departments, and hospitals as an appropriate sequel to the guide for maternal death studies.[2] It is believed that wide use of such material will expedite the prevention of avoidable deaths and will stimulate interest in efforts to further reduce both maternal and perinatal mortality and morbidity.

The first report in this series by the Committee (see under Council on Medical Service, page 1124, this issue) will describe the pioneering work of the Philadelphia group in its study of neonatal mortality. The experiences of medical groups in other areas will be described in succeeding reports. The Committee's purpose in publishing these articles is to help acquaint the medical profession with what is being done in various areas. The methods and results of these many local and state programs will be studied and compared, and the techniques that are considered most effective will be incorporated into the study guide. Regional meetings have been held for discussion and agreement on many points involved. Other meetings are planned in order to collate findings; and additional regional meetings are anticipated as a means to disseminate information and stimulate interest in further efforts to lower perinatal mortality and morbidity.

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[1] Annual Summary for 1956, part 2, Estimated Numbers of Deaths and Death Rates for Selected Causes: United States, 1956, *Vital Statistics Monthly Reports* 5:13 (May 10) 1957.

[2] Guide For Maternal Death Studies with Causes of Obstetric Deaths, Direct and Indirect, and Reports on Study of Seven Programs, Committee on Maternal and Child Care, Council on Medical Service, A. M. A., 1957.

ORGANIZATION SECTION

BLUE SHIELD AND EDUCATION

What are the effects of Blue Shield on graduate medical education? Dr. Edward L. Turner, Secretary of the Council on Medical Education and Hospitals, and Dr. Ward Darley, executive director of the Association of American Medical Colleges, attended a meeting, in Chicago, with representatives of Blue Shield several weeks ago when some problems that have been associated with the development of prepaid insurance were discussed in the light of graduate medical education. The conferees concluded that this area is deserving of cooperative study by the AAMC, the A. M. A. Council on Medical Service and Council on Medical Education and Hospitals, and other organizations which might be involved. "It is inevitable," said Dr. Turner, "that this general field involving prepayment will, as time goes by, become of increasing concern to medical education in all of its phases—as well as to medical care itself."

HOSPITAL MEDICAL EDUCATION

The feasibility of establishing a broad educational program for hospital directors of medical education was discussed recently at a meeting in Chicago. In attendance were representatives of the A. M. A. Council on Medical Education and Hospitals, the American Hospital Association, and the Association of Hospital Directors of Medical Education. The group recommended that, as a first step, 20 to 25 individuals experienced in the field of education gather together at an "invitational workshop" to study need, relationships, types of training, and directorial qualifications in hospital medical education programs. An advisory committee was to be established to work out further details.

MEETING ON WARNING ON CHEMICAL PRODUCTS

The Committee on Toxicology will conduct a meeting July 25 at A. M. A. headquarters, in Chicago, to discuss proposed legislation requiring the declaration of hazardous ingredients and warning statements on the label and in the accompanying literature of household, commercial, and industrial chemical products. Representatives of interested industries and trade associations also will attend. Further information may be secured from the Committee at A. M. A. headquarters.

FILMS OF THE SAN FRANCISCO MEETING

Filmed highlights of the 107th A. M. A. Annual Meeting—presented by the American Medical Association in cooperation with Merck, Sharp & Dohme—will be available after Sept. 1, for showing to medical meetings. Entitled "San Francisco—1958" (television abstracts of the A. M. A. Annual Meeting), the 40-min. black and white films taken from kinescopes of five daily television programs may be secured from either the A. M. A. Film Library or Merck, Sharp & Dohme, Philadelphia. These programs will feature interviews with speakers on the convention program.

EXHIBIT ON FITNESS

"Seven Paths to Fitness" is the title of a new A. M. A. exhibit to be shown first at the Public Relations Institute, Aug. 27-28, in Chicago. Sponsored by the Bureau of Health Education in cooperation with the Bureau of Exhibits, the display emphasizes the seven avenues to health and fitness: nutrition, relaxation, play, exercise, dental care, medical care, and work. Over-all murals depict the sources and activities in each category. The exhibit is primarily intended for professional audiences having a direct interest in physical fitness. It will be available for bookings after Sept. 1, through the Bureau of Exhibits. A smaller type exhibit on the same subject will be completed later.

CHANGE OF ADDRESS

If you change your address please notify The Journal at least six weeks before the change is made. Include the address label clipped from your latest copy of The Journal, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

MEDICAL EDUCATION IN PUERTO RICO

A recent survey of intern and residency training programs in Puerto Rico indicates the carrying out of good teaching programs and an intense interest and enthusiasm to teach on the part of attending staffs. Dr. Arthur N. Springall, Assistant Secretary of the A. M. A. Council on Medical Education and Hospitals, reported on a study of a total of 17 facilities—including government hospitals, the medical school of the University of Puerto Rico, the Veterans Administration Hospital, and some private institutions on the island. He found that medical records in Puerto Rico hospitals compare favorably with those of teaching hospitals on the continent, that there is considerable interest in multiphasic rehabilitation of patients, and that there is a wealth of clinical material available for study. There also is a need for pathologists on the island. A new medical center is being planned for San Juan, with construction of one new unit expected to begin in a few weeks. Dr. Springall reported that a majority of house staffs are native Puerto Ricans graduated from Spanish and Mexican medical schools.

COUNCIL ON MEDICAL SERVICE

STUDY OF PERINATAL MORTALITY AND MORBIDITY PROGRAMS IN THE UNITED STATES

PART 1

PHILADELPHIA NEONATAL MORTALITY STUDY

Closely related to the study of maternal deaths in Philadelphia, which began in 1930, was a study of neonatal deaths. The latter was initiated in 1931 by a subcommittee of the Maternal Mortality Committee of the Philadelphia County Medical Society in cooperation with the Philadelphia Department of Public Health.

Because of a shortage of personnel during World War II and the departure of certain key individuals, the study lapsed in activity. However, at the request of the Philadelphia County Medical Society, a Philadelphia Neonatal Study Committee was established in 1946, with members representing the medical schools and hospitals of Philadelphia. Later this committee was reorganized into one of the active coordinating committees of the medical society in cooperation with the local obstetric and pediatric societies. Its purpose in studying the problems of the neonatal period is to discover the causes of neonatal deaths and the preventable factors involved, to reduce thereby the number of such deaths, and to further understanding of the causes of prematurity.

The membership of the committee consists of a representative from the pediatric department of each of the 48 hospitals. Its chairman is appointed by the president of the county medical society upon the recommendation of the local pediatric society. It is informally understood that each chairman, if he is willing, will serve for about 10 years to assure continuity of the programs. A steering committee of 12 is appointed from the members of the full committee by the president of the county medical society upon the recommendation of the chairman for staggered four-year terms. It has been the policy to include at least one representative from each of the five teaching institutions. The secretary of the Neonatal Study Committee is a staff member of the maternal and child health section of the Philadelphia Department of Public Health.

Scope of Study

All deaths in Philadelphia of infants less than 28 days old are included in the study. Matching of birth and death certificates, which was started in 1953, makes it possible for all neonatal deaths to be classified by the hospital of birth. The committee does not study morbidity as such, but topics discussed at open committee meetings have included management of erythroblastotic infants, fluid and electrolyte balance, early detection of congenital defects and preventable surgical procedures. As the need arises ad hoc subcommittees are appointed on such matters as prematurity and hospital nursery records.

This is the first of a series of articles prepared by the Committee on Maternal and Child Care of the Council on Medical Service on perinatal mortality and morbidity study programs that are being conducted in various parts of the United States. Subsequent articles will appear in THE JOURNAL from time to time.

Committee members are W. L. Crawford, M.D., *Chairman*, Rockford, Ill.; R. B. Chrisman Jr., M.D., Coral Gables, Fla.; Philip S. Barba, M.D., Philadelphia; Harold S. Morgan, M.D., Lincoln, Neb.; Garland D. Murphy, M.D., El Dorado, Ark.; Howard A. Nelson, M.D., Greenwood, Miss.; J. L. Reichert, M.D., Chicago; Donald A. Dukelow, M.D., Consultant, Chicago; and Mr. George W. Cooley, Secretary, and Mr. Donald B. Berg, Research Assistant, Chicago.

Method of Operation

Case-finding and Collection of Data.—Through the cooperation of state and local health departments, transcripts of the neonatal death certificates for Philadelphia are sent to the committee secretary's office in the maternal and child health section. Prior to July 1, 1955, the secretary's office would send a study form to the hospital where a neonatal death occurred, with the request that it be filled out by the committee hospital representative or a person designated by him and returned as promptly as possible. This voluntary reporting rose from 60% in the earlier years of the study to almost 95% in 1955. Since July 1, 1955, a supply of study forms has been regularly sent to each hospital representative. The forms are filled out by the attending physician and the residents, interns, and other hospital personnel acquainted with the particular neonatal death and are submitted to the hospital representative for review and forwarding to the committee secretary. Periodically, each hospital representative is sent a list of the neonatal deaths for which completed forms have not yet been received. Also, individual physicians known to be familiar with the case are requested to supply pertinent information which may not be available from the hospital records. Standardized forms are also used for these contacts.

Processing of Data.—Until recently the steering committee reviewed each case individually, decided the cause of death, and determined the rating of responsibility. Since these deaths number about 1,200 annually, several specially trained physicians of the maternal and child health section of the department of public health now screen the study forms, leaving only unusual or controversial cases to be decided by the steering committee. These physicians code the data which is subsequently transferred to punch cards for statistical analysis. Anonymity is assured; the hospital representative, the committee secretary, and the physician who codes the questionnaire are the only persons who know the names appearing on the study form except in cases discussed by the whole steering committee. These study forms are kept on file in the health department as privileged and confidential material.

As may be seen from the foregoing, close working relationships are maintained between the Philadelphia County Medical Society, the Philadelphia Department of Public Health, the Philadelphia Pediatric Society, and the Obstetrical Society of Philadelphia. This cooperation extends to the financing and use of facilities. Space is provided at both the County medical society building and the department of public health for a secretary who functions in both offices. Meeting rooms are provided by the medical society, which also furnishes office supplies and equipment, postage, etc. The medical society has shared the expense of sending a representative to national and other meetings, and it has also shared the cost of exhibits. The department of public health in turn supplies staff for preparation of reports, provides the services of a statistical consultant (on a limited basis), supplies report forms and tabulation cards, secures and distributes reprints, manuals, and books, and pays the costs of mailing meeting notices and other material as well as general administrative and clerical costs.

The steering committee meets about three or four times a year to set policies, develop programs, and review selected unusual or controversial neonatal deaths. At these meetings preparations are made for the regular bimonthly open luncheon meetings of the full committee. All hospital representatives are sent invitations and, in addition, notices inviting interested physicians, nurses, medical students, interns, and residents are sent to each hospital for posting. Attendance ranges from 30 to 50. At these bimonthly meetings one or more cases are presented to illustrate such particular topics as pulmonary hyaline membrane, management of the small premature infants, or Rh incompatibility. Bimonthly joint open meetings are also held with the Maternal Welfare and Fetal Death committees for discussion of neonatal deaths with obstetric implications. These joint meetings also discuss the rating of responsibility. All neonatal deaths are classified according to the International Statistical Classification of Diseases, Injuries, and Cause of Death[1] and are rated as probably preventable, nonpreventable, or unclassifiable. Where deaths are rated as probably preventable they are classified as antenatal (obstetric), postnatal (pediatric), or combined and are assigned more specifically to (1) inadequate prenatal care, (2) the fault of the family, (3) physician's error in judgment, (4) physician's error in technique, (5) intercurrent disease, and (6) unavoidable disaster.

Follow-up and Use of Findings.—A yearly report of neonatal mortality (by hospital) is sent to each hospital's administrator, medical superintendent, president of the board of trustees, chairman of the staff, head of the obstetric department, head of the pediatric department, head of nurses, chief obstetric nurse, and the hospital representative on the Neonatal Study Committee. Hospital names are omitted except for that of the hospital receiving the report; the listing is, rather, by numbers of live births. Also given are the number of neonatal deaths and the rate (with standard deviation) per 1,000 live births. Administrators of hospitals with rates higher than the city's average receive a personal follow-up letter from the health commissioner, with copies sent also to the heads of obstetrics and pediatrics. This letter, which points out that no criticism is intended, indicates the willingness of the health department through its maternal and child health section to arrange meetings of consultants with personnel of the hospital to help solve any problems regarding neonatal mortality and morbidity. Replies to these letters have been appreciative, and several hospitals have asked for conferences.

Reports to the profession are published in the county medical society's journal at frequent intervals and also in state and national journals. Reports to the public on the activities of the committee appear from time to time in newspaper editorials and articles. The hospital council also publicizes committee activities through its newsletter. Hospital staff members are urged to discuss each neonatal death at their regular meetings. The committee's findings are also used for teaching purposes in the five local medical schools.

A review committee has been established consisting of the chairman of each of the three mortality study committees, a representative of the department of public health, and a representative of the hospital association. The purpose is to coordinate activities, review policies, and look for ways and means to improve the effectiveness of their study programs.

TABLE 1.—*Neonatal Deaths and Death Rates, Philadelphia, Selected Years, 1940-1956**

Year	Live Births, No.	Neonatal Deaths, No.	Deaths/1,000 Live Births
1940	31,227	846	27.1
1945	38,825	976	25.1
1950	47,516	1,058	22.1
1951	50,318	1,054	20.9
1952	51,661	1,113	21.5
1953	51,706	1,162	22.5
1954	53,716	1,252	23.3
1955	52,368	1,305	24.9
1956	53,203	1,236	23.2

* Data supplied by the office of Statistics and Research, Philadelphia Department of Public Health.

Results

The statistical data in the following paragraphs are from the office of statistics and research of the Philadelphia Department of Public Health.

Analysis of the 1953 statistics revealed that about 70% of the neonatal deaths were in premature infants (2,500 Gm. or less). Ninety per cent occurred during the first week and over 50% on the first day. In individual hospitals the neonatal death rates ranged from 8.4 to 44.6 per 1,000 live births.

Table 2, which presents the causes of neonatal death in Philadelphia in 1953, shows that the category "injury at birth" accounts for over one-fourth of the total. This category (injury at birth, 760-761, in the International Classification) includes many more clinical diagnoses and obstetric situations than clinicians are usually aware. The term is apt to be associated only with such iatrogenic factors as intracranial hemorrhage following prolonged labor or application of high forceps. Also in this category, however, are compression, prolapse, knot or strangulation of the umbilical cord; placenta previa; precipitate birth; abnormal presentation (breech, foot, tranverse, etc.); version; and such conditions as edema of the brain.

TABLE 2.—*Causes of 1,162 Neonatal Deaths, Philadelphia, 1953*

Causes*	Premature † No.	Premature † %	Full-term ‡ No.	Full-term ‡ %	Birth Weight Unknown, No.	Total No.	Total %
Postnatal asphyxia and atelectasis (762)	185	22.6	38	11.8	7	230	19.8
Injury at birth (760,761)	208	25.5	98	30.6	4	310	26.7
Congenital malformation (750-759)	48	5.9	80	24.9	1	129	11.1
Infection of newborn infant (763-768)	55	6.7	41	12.8	0	96	8.2
Blood dyscrasias (770,771)	16	2.0	25	7.8	2	43	3.7
Prematurity (774,776)	244	29.9	3	0.9	5	252	21.7
All other known causes (769,772,773)	39	4.8	24	7.5	2	65	5.6
Unknown cause	21	2.6	12	3.7	4	37	3.2
Total	816	100.0	321	100.0	25	1,162	100.0

*According to International Statistical Classification of Diseases, Injuries, and Causes of Death (6th revision), with International Classification number given in parentheses.

† 2,500 Gm. or less.

‡ More than 2,500 Gm.

Prematurity (mostly unqualified) is the second highest cause (21.7%) of neonatal death, with postnatal asphyxia and atelectasis ranking third (19.8%) (table 2). It should especially be noted that 30.6% of the neonatal deaths in full-term infants were due to birth injury, as were 25.5% of the deaths in infants. Also of special interest is the fact that postnatal asphyxia and atelectasis caused twice as many neonatal deaths among premature as among full-term infants.

TABLE 3.—*Survival of Premature Infants, Philadelphia, 1953*

Birth Weight, Gm.	Live Births, No.	Neonatal Deaths, No.	Survival, %
1,000 or less	325	325	0.0
1,001-1,500	397	210	47.1
1,501-2,000	860	166	80.7
2,001-2,500	2,896	115	96.0
Total	4,478	816	81.8

No premature infants weighing under 1,000 Gm. survived the neonatal period (table 3), and the over-all premature neonatal mortality was 18.2%. Table 4 shows the wide range between the neonatal mortality rate in the weight groups and the total rates for neonatal deaths in whites and nonwhites.

It should be noted that the 23.1% nonwhite births in 1953 accounted for 35.4% of the neonatal deaths. (Analysis of 1954 and 1955 data will soon be available.)

Comments and Conclusions

The Neonatal Study Committee, through its detailed study and analysis of neonatal deaths in cooperation with the Philadelphia Department of Public Health, has been able to define specific problems and is now initiating programs to solve them. Steps are being taken to assure more adequate prenatal care as one means of reducing the number of prematurely born infants; it is in this group (8.7% of all live births in 1953) that 70% of the neonatal deaths occur. The committee, in cooperation with the department of public health, is working to establish better facilities for care of premature infants in the larger hospitals, reception centers for such infants in strategic locations throughout the city, in-training courses for nurses, and a center to provide training for hospital teams of physicians and nurses in modern methods of caring for premature infants.

TABLE 4.—*Neonatal Mortality, Premature and Full-term, Philadelphia, 1953*

Birth Weight	No. of Live Births	No. of Neonatal Deaths	Deaths/1,000 Live Births
1,000 Gm. or less	325	325	1,000.0
2,500 Gm. or less	4,475 (8.7%)	816	182.2
2,501 Gm. or more	47,206	321	6.8
Unknown	25	25	1,000.0
Total	51,706	1,162	22.5
White	39,725 (76.9%)	751	18.9
Nonwhite	11,981 (23.1%)	411	34.3

The committee recommends that each hospital survey its nursery facilities and procedures and make whatever changes and improvements are necessary to conform with the Standards and Recommendations for Hospital Care of Newborn Infants, published by the American Academy of Pediatrics.[2] It also recommends that each hospital make every effort to determine the exact cause of each death through autopsy performed by a pathologist well acquainted with pathological conditions in newborn infants. The committee urges that each hospital discuss its neonatal deaths at meetings attended by the staff obstetricians, pediatricians, pathologists, and nursing personnel and that such meetings classify each case as to responsibility and preventability. The maternal and child health section of the department of public health has expert, experienced obstetricians and pediatricians available for consultation to assist hospitals with their improvement programs. The committee seeks the active cooperation of all concerned to achieve its goal—the reduction of neonatal deaths by determining true causes and the possible avoidable factors involved.

Emphasis in the Philadelphia neonatal study has been chiefly on professional education through free discussion and general reports to physicians and hospital administrators. The effectiveness of this program is suggested by the growing local interest and participation in the study. In 1955, 94.6% of the 1,252 neonatal deaths were voluntarily reported. Several large neighboring hospitals outside the official health juridiction have asked to participate, and others have indicated their interest.

References

1. Manual of The International Statistical Classification of Diseases, Injuries, and Causes of Death, Sixth Revision of the International Lists of Diseases and Causes of Death, World Health Organization, Geneva, Switzerland, vol. 1, 1948, pp. 212-218.

2. Standards and Recommendations For Hospital Care of Newborn Infants, Full-term and Premature, American Academy of Pediatrics, 1954, revised 1957.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

APPOINTMENT OF ASSOCIATE SECRETARY

The Council on Medical Education and Hospitals has announced the appointment of Dr. John C. Nunemaker as Associate Secretary of the Council as of Aug. 1. Dr. Nunemaker will be in charge of the graduate education aspects of the work of the Council dealing with internships and residencies.

Dr. Nunemaker, a native of Colorado, after receiving an M.D. from Harvard University in 1937, was on the house staff at Peter Bent Brigham Hospital in Boston and later an Assistant in Medicine at John Hopkins University. He served four years in the Army, having been Commanding Officer of a Station Hospital in Cairo, Egypt, and Surgeon of the Middle East Service Command. After this, he became Chief of the Medical Service, Veterans Administration Hospital, Salt Lake City, and Assistant Professor of Medicine, University of Utah College of Medicine. He went to Washington, D. C., in 1952, to head the Veterans Administration Research Service, after which he was appointed Director of Education and Service. Dr. Nunemaker is a Diplomate of the American Board of Internal Medicine and a member of the Government's Interdepartmental Committee on Scientific Research and Development.

MEDICAL NEWS

CALIFORNIA

Gift for Memorial Laboratories at Stanford.—Establishment of the William A. Ross Memorial Laboratories in the Medical Center under construction on the Stanford University campus after an initial gift of $100,000 from Mr. Ross' widow, has been announced. Initially the laboratories will be devoted to heart research. They will be constructed in the department of medicine, headed by Dr. David A. Rytand, in the clinic building, one of five buildings in the first stage of Stanford Medical Center construction. Mr. Ross, who was president of Columbia Steel Company, died in 1949.

Society News.—The California Society of Plastic Surgeons has elected the following officers: president, Dr. Gerald H. Gray, Oakland; vice-president, Dr. George V. Webster, Pasadena; historian, Dr. James B. Johnson, Beverly Hills; and secretary-treasurer, Dr. Richard A. Shepard, Oakland.——East Bay Psychiatric Association officers for 1958 are as follows: Dr. William M. McGaughey, Oakland, president; Dr. Richard L. Sutherland, Oakland, president-elect; Dr. Alan S. Mariner, San Leandro, secretary; Dr. Frederick R. Ford, Berkeley, treasurer.

CONNECTICUT

Dr. Kirchner Receives Mosher Award.—Dr. John A. Kirchner, associate professor of otolaryngology, Yale School of Medicine, New Haven, has received the annual Harris P. Mosher award in recognition of his work with the cricopharyngeus and its connection to the nervous system. This award is given by the American Laryngological, Rhinological, and Otological Society.

Personal.—Dr. Allan J. Ryan, Meriden, has been named literary editor of the *Connecticut State Medical Journal* by the council of the State Medical Society, to succeed Dr. Harold M. Marvin, New Haven, who resigned.——Dr. Louis P. Hastings, Hartford, has been reappointed to the Connecticut Medical Examining Board by Governor Ribicoff following recommendation by the State Medical Society. Dr. Hastings has served on the board for 10 years. He is full-time pathologist at St. Francis Hospital, Hartford.

Hospital News.—Renovation of the outpatient department of the Hospital of St. Raphael, New Haven, has been completed, and a formal opening for the public was held May 16. The 26-clinic department has new floors, ceilings, lighting fixtures, and structural changes to enlarge treatment, waiting, and interviewing space. Of the $158,000 spent for these improvements and equipment, $152,000 was a grant from the Ford Foundation. Other changes include air-conditioning of the hospital's surgical suite, enlargement of the surgical suite's recovery room, and renovation of the x-ray department, including equipment, totaling $130,000.

DISTRICT OF COLUMBIA

Appoint Chairman of Department of Medicine.—Dr. Lawrence H. Kyle, professor of medicine, Georgetown University School of Medicine, has been appointed chairman of the department of medicine, effective July 1, succeeding Dr. Hugh H. Hussey Jr., who will relinquish the post to become dean of the School of Medicine. Dr. Kyle joined the Georgetown faculty as a research fellow in endocrinology. In 1948 he was made William Wade Hinshaw Cancer Research Fellow and was appointed instructor in medicine. He has been director of the metabolic clinic of Georgetown University Hospital since 1943 and has been director of the metabolic laboratories since 1950. Dr. Kyle is a diplomate of the American Board of Internal Medicine (1951).

ILLINOIS

St. Francis Hospital Expansion Program.—St. Francis Hospital, Evanston, broke ground for a $5,630,000 expansion of the present building June 10. Construction of an extension along the front of the hospital and two extensions at the rear will provide 125 additional beds for patients and the enlargement of all departments. The outpatient department, emergency room, x-ray and laboratory sections will be relocated for easy access by patients. An expanded surgical pavilion will be included. The maternity division with newborn nurseries will be relocated and modernized and a large premature nursery provided. Funds for the expansion will be sought in a public campaign to be launched this fall. The public goal is $3,000,000. The Ford Foundation has given $230,100. The last addition to the hospital, now a 385-bed institution, was in 1928. The interns' residency was constructed in 1952. St. Francis was founded in 1900.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Chicago

Regulations for Reporting Blood Involvements.—In accordance with the recommendation of the Joint Maternal Welfare Committee of Cook County, the Chicago Board of Health has approved the following regulations:

> It shall be the duty of every physician, laboratory, and hospital to report immediately to the Chicago Board of Health by telephone Rh negative mothers with a current pregnancy and to confirm it in writing within 24 hours.
>
> It shall be the duty of every physician and hospital to report immediately to the Chicago Board of Health by telephone the birth of infants with hemolytic disease of the newborn and to confirm it in writing within 24 hours.

When confirming a report, physicians should write to the Chicago Board of Health, 54 W. Hubbard St., Hospital Audit Unit.

University News.—Prof. Etienne Wolff, of the Collège de France, Paris, presented "Growth of Human and Other Mammalian Cancers on Chick Embryo Organs in Vitro" and "Production of Monstrosities by X-rays and Their Prevention," the latter as a "George Shkoler Memorial Lecture," June 3 and 4, sponsored by the Mount Sinai Medical Research Foundation and The Chicago Medical School.——John P. Scott, Ph.D., chairman, Division of Behavior Studies at the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine, since 1945, joined the department of psychology in the Division of Biological Sciences of the University of Chicago April 1 as visiting professor for the quarter ending June 30.

INDIANA

Dr. Kohlstaedt Honored.—Dr. Kenneth G. Kohlstaedt, director of Eli Lilly and Company's clinical research division, Indianapolis, has received the first Certificate of Appreciation for Meritorious Service to be awarded by the American Academy of General Practice. The award was established by resolution of the A. A. G. P.'s Congress of Delegates at the 10th annual scientific assembly recently. Dr. Kohlstaedt was recommended for the award by the academy's Indiana chapter "in appreciation for the invaluable service . . . rendered the Academy for a number of years." He is an honorary member of the Indiana chapter.

Dr. Lilly Receives Pharmaceutical Medal.—Eli Lilly, LL.D., chairman of the board of directors of Eli Lilly and Company, has been selected by the past-presidents of the American Pharmaceutical Association to become the recipient of the 1958 Remington Honor Medal, established by the New York Branch of the association in 1918, "to be presented annually to the individual who has done most for American Pharmacy in the previous year, or whose continuing contributions to the advancement of the profession over a period of years have been most outstanding." In August, 1953, Dr. Lilly was elected honorary president of the association, which marked the first time the A. Ph. A. has given the honorary presidency to a father and son. Dr. Lilly's father was similarly honored in 1934.

KENTUCKY

Medical Scholarship Fund.—Twenty-eight students were added to the list of those receiving aid in financing their medical educations from the Rural Kentucky Medical Scholarship Fund at a recent meeting of its board of trustees, according to an announcement from Dr. Carl C. Howard, Glasgow, chairman of the board. Sponsored by the Kentucky State Medical Association, the fund is aimed at distributing adequate medical care to rural Kentuckians and helping worthy students interested in rural practice to gain a medical education. Since its inception in 1946, it has aided 137 students with 335 loans amounting to nearly $257,000. Currently 22 of the recipients are fulfilling their obligations to the fund by practicing in rural Kentucky areas, 14 are continuing their practice after fulfilling their obligations later, 13 are completing internships and residencies, and 47 are in medical schools. The board of trustees administers the fund, which in recent years has been aided by grants from the state legislature.

LOUISIANA

Dr. Paterson Named Department Chairman.—Dr. John C. S. Paterson, associate professor of medicine, Tulane University of Louisiana School of Medicine, New Orleans, will become chairman of the department of tropical medicine and public health July 1. Dr. Paterson is a native of Scotland. He came to the U. S. in 1949 to attend the University of Rochester in New York under a Commonwealth Fund fellowship. He returned to the University of London as tutor in medicine until he joined the faculty at Tulane in 1953. Dr. Paterson was awarded the M.D. degree with commendation in 1956 for his thesis on diurnal variations in the metabolism of iron. He has done research in sickle-cell disease, metabolism of iron, cerebral circulation, and epidemiology of leukemia. Dr. Paterson's wife, Dr. Ruth D. Paterson, assistant professor of neurology at Tulane, is also a member of the Royal College of Physicians, London.

Extend Consultant Services to South America.—Tulane University, New Orleans, has contracted with the International Cooperation Administration to extend its consultant services to the seven medical schools of Colombia, South America, for three more years. In 1955 at the request of the Colombia medical schools the project was begun to provide advice to the Colombian schools in making changes in the medical curriculum and to strengthen basic medical science teaching. Five Tulane consultants have spent three months each in Colombia, and opportunities have been extended to Colombian physicians to come to the U. S. on fellowships for advance study. Partly as a result of this program, 22 Colombian students and faculty members have been in training at Tulane during the past year and others have been aided in getting support to study in medical centers throughout the country. Direct results of the program include the establishing of an enterobacteriological center in Cali and a cooperative research project to investigate the clinical significance of various tropical parasites.

MASSACHUSETTS

Dr. Lee and Professors Emeriti Honored.—Ceremonies honoring Dr. Roger I. Lee, first acting dean of the faculty of public health at Harvard University, Boston, and a past-president of the American Medical Association, and the professors emeriti of the School of Public Health were held May 28. Citations honoring Dr. Lee and each of 10 professors emeriti were presented by members of the faculty. In addition to Dr. Lee, the guests of honor included:

> Dr. Alice Hamilton, Hadlyme, Conn., Dr. Frederick Fuller Russell, Louisville, Ky., Dr. Ernest Edward Tyzzer, Wakefield, Mass., Edwin Bidwell Wilson, Ph.D., Brookline, Dr. Richard Mason Smith, Boston, Dr. George Cheever Shattuck, Brookline, Melville Conley Whipple, Tamworth, N. H., Dr. Harold Coe Stuart, Chestnut Hill, Dr. Franz Goldman, New Rochelle, N. Y.

MICHIGAN

Dr. Neafie Honored.—Dr. Charles A. Neafie, for 40 years a health officer in Pontiac, received from the Michigan Health Officers Association May 8 a *distinguished health service award*. Dr. Neafie is a past-secretary and past-president of the Oakland County Medical Society and former member of the council of the Michigan State Medical Society. The Michigan Health Officers Association also made Dr. Neafie "president for a day" of the association.

Increase Enrollment at Wayne.—With legislative approval, Wayne State University's board of governors has voted to increase the College of Medicine enrollment from 75 to 125 freshmen students, beginning in September. Funds to cover expansion will come from the state's general appropriation to the university of $9,718,900. Estimated cost for the additional students is $285,000 for the first year. By 1962, the total medical school enrollment is expected to be 500, compared with the present 300. The university's action climaxed a concerted two-year effort by a group of lawmakers and health officials to head off a growing shortage of doctors in Michigan. That expansion of Wayne's College of Medicine could be done practically and economically was substantiated by a report to a legislative study committee on higher education by William T. Sanger, Sc.D., chancellor of the Medical College of Virginia, Richmond. The report said that Wayne's medical school should be expanded to accommodate 200 entering students a year before consideration is given to a third medical school in Michigan.

NEW YORK

Permits for Farm Labor Camps.—Owners of more than 1,060 farm labor camps in New York State reportedly are affected by an amendment of the Public Health Law which requires that permits be obtained to operate such camps. Dr. Herman E. Hilleboe, State Health Commissioner, announced that the State Legislature enacted the amendment and that the provisions for the permits are outlined in the State Sanitary Code, which sets up specific requirements concerning housing, fire hazards, bathing and toilet facilities, food handling and food storage facilities, water supply, and sewage disposal at farm labor camps. A new permit must be obtained each year before a farm labor camp is opened. Camps are inspected regularly to insure compliance with the Sanitary Code regulations. Information may be obtained from the State Health Department, 84 Holland Ave., Albany 8, N. Y.

New York City

Science Writing at Columbia.—Columbia University's advanced science writing program will start in September on an enlarged scale made possible by a 3-year $100,000 grant from the Rockefeller Foundation. The pilot financing was a 2-year, $70,000 grant from the Alfred P. Sloan Foundation. The combined financial support provides for 6 to 8 fellowships the first year and 10 or more in each of the two following years. The stipends will cover, in addition to tuition and fees, up to about $4,400 travel and living expenses for the academic year. In general the program will include participation in regular or specially arranged science courses or seminars under Columbia's faculties of pure science, medicine, or engineering; organized study of selected research and developments projects in the New York area; special meetings with both university and industrial research leaders; and special writing, some of it for publication. All participants will be expected to undertake a major research writing project in addition to regularly assigned writing.

Dedicate Mental Health Clinic.—Dr. Gunnar Gunderson of LaCrosse, Wis., President-Elect of the American Medical Association, addressed a service of dedication for the Mental Health Clinic of the Lutheran Medical Center in Brooklyn recently. Opened last September, the clinic is directed by Dr. Paul A. Qualben, a psychiatrist, and John P.

Kildahl, Ph.D., a psychologist, both, also ordained pastors of the Evangelical Lutheran Church. The clinic is now providing about 45 hours per week of treatment to persons from all sections of the metropolitan New York area. It conducts a program of community education through lectures to local groups and seminars for clergy. Other participants in the dedicatory service were Dr. Thurman B. Givan, president, New York State Medical Society; F. Eppling Reinartz, president, National Council; and the Rev. C. O. Pedersen, president, Atlantic Circuit, Evangelical Lutheran Church. The Lutheran Medical Center includes a general hospital, maternity ward, nursing school, an intern program, and 14 other clinics.

PENNSYLVANIA

Philadelphia

Appoint Chairman of Anatomy Department.—Andrew J. Ramsay, Ph.D., has been appointed professor and head of the department of anatomy and director of the Daniel Baugh Institute of Anatomy of Jefferson Medical College. Dr. Ramsay served as an assistant and instructor in histology and embryology at Cornell University, New York City, from 1930 to 1936. He became assistant professor of embryology at Jefferson Medical College in 1937, associate professor in 1941, and professor in 1948.

Grant for Cancer Research.—The Fels Research Institute of the Temple University School of Medicine has been awarded a grant of $195,488 for its next fiscal year beginning July 1 by the Fels Fund. The institute, established by the late Samuel S. Fels, of Philadelphia, is dedicated to research in gastroenterology and cancer. An additional grant of $29,000 has been awarded the institute by the Fels Fund toward the cost of a new laboratory, now nearing completion. The institute is under the direction of Dr. Harry Shay, professor of clinical medicine at Temple University.

Medical Arrangements for Orchestral Tour.—To insure the health of Philadelphia Orchestra members during the eight-weeks' tour to 14 countries overseas, the orchestra has taken along its personal physician, Dr. Milton J. Freiwald, ophthalmologist on the faculty of Jefferson Medical College. The president of Merck, Sharp and Dohme presented a medical case to Conductor Eugene Ormandy and Dr. Freiwald prior to the orchestra's departure May 10. The case contained drugs for emergencies and a surgical kit. With aid of the city's health department, orchestra personnel were inoculated for smallpox, typhus, and typhoid. Dr. Freiwald has had the assistance in these arrangements of Dr. George F. Lull, secretary of the American Medical Association; Dr. Paul Van de Calseyde, director of the World Health Organization in the United Nations regional office, Copenhagen; and Dr. Louis H. Bauer, secretary general, World Medical Association, New York City.

GENERAL

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	May 31, 1958		June 1, 1957
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	1	1	..
Middle Atlantic States			
New York	..	1	1
New Jersey	..	..	..
Pennsylvania	..	..	..
East North Central States			
Ohio	..	..	1
Indiana	..	..	..
Illinois	1	4	..
Michigan	..	..	3
Wisconsin	..	..	..
West North Central States			
Minnesota	..	..	..
Iowa	..	1	..
Missouri	..	..	1
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	..	..	..
Kansas	..	..	1
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	1	1	2
West Virginia	..	..	..
North Carolina	..	1	..
South Carolina	..	..	2
Georgia	..	..	..
Florida	3	7	..
East South Central States			
Kentucky	..	..	1
Tennessee	1	1	..
Alabama	..	..	..
Mississippi	..	1	3
West South Central States			
Arkansas	..	..	2
Louisiana	..	..	4
Oklahoma	2	5	1
Texas	4	11	32
Mountain States			
Montana	..	..	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	1
New Mexico	..	..	..
Arizona	..	1	2
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	..	..
Oregon	..	..	1
California	4	6	6
Territories and Possessions			
Alaska	..	..	..
Hawaii	4	4	..
Puerto Rico	1	1	..
Total	22	46	64

Six-Member Society Strong on Civic Duty.—The Bosque County Medical Society (Texas) has a membership of six doctors and they are holding—or have held—27 positions in local government, business, and civic life. Among the six are a past-president of the Texas Board of Education, a former mayor, two school board trustees, two city council members, two bank directors, a director of Texas Good Roads Association, and a finance company director. Altogether, they put in over 140 hours a month in civic activities.

Awards to Rehabilitation Workers.—Fellowship and scholarship awards for the specialized training of 34 professional workers who are giving rehabilitation services to the crippled have been announced by the National Society for Crippled Children and Adults and two national women's fraternities, Alpha Chi Omega and Alpha Gamma Delta. Alpha Chi Omega financed 14 scholarship awards to doctors, therapists, teachers, administrators, and other specialists to take advanced specialized training for work with the cerebral palsied at five medical schools, hospitals, and universities this summer. Alpha Gamma Delta provided funds for 20 fellowships to counselors, guidance teachers, employment interviewers, placement personnel, and other professional workers who will receive specialized training in counseling and placement of severely handicapped persons including those with cerebral palsy in a special four-week training course at the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, June 16-July 11.

Institute for Muscle Disease in New York City.—Construction started recently on a $3,700,000 Institute for Muscle Disease following ground-breaking ceremonies attended by civic officials and officers and members of Muscular Dystrophy Associations of America, Inc., which is sponsoring the institute. The structure is located on 71st Street between York Avenue and East River Drive in Manhattan. The institute will conduct research and correlate medical data from other sources toward finding a cause and cure for muscular dystrophy and related diseases. MDAA officials participating in the ceremony included president William Mazer and Dr. Ade T. Milhorat, chairman of the MDAA medical advisory board. The institute was made possible through public contributions to the November "March for Muscular Dystrophy." The general laboratories, occupying 5 of the 11 floors, are so arranged that alterations to meet future needs can be made with a minimum of expense. The building will be air-conditioned throughout. A program of research presently maintained by MDAA includes nearly 100 research projects in this country and abroad. The association also provides clinical care and patient services through its chapters.

Society News.—The **American Urological Association** has elected the following officers: president, Dr. Adolph A. Kutzmann, Los Angeles; president-elect, Dr. William M. Coppridge, Durham, N. C.; secretary, Dr. Samuel L. Raines, Memphis, Tenn.; treasurer, Dr. Grayson L. Carroll, St. Louis; and historian, Dr. Wirt B. Dakin, Los Angeles. The 1959 meeting will be held in Atlantic City, N. J., April 20-23, with headquarters at Chalfonte-Haddon Hall.——The **Southern Neurosurgical Society** has made the following officer changes: Dr. James G. Arnold Jr., of Baltimore, succeeded Dr. William F. Meacham, of Nashville, as president; Dr. Charles L. Neill, of Jackson, was elected vice-president; the secretary-treasurer, Dr. C. Douglas Hawkes, of Memphis, has one more year of a three-year term to serve. The 11th annual meeting of the society will be held at the Americana, Bal Harbor, Miami Beach, Fla., Jan. 23-24, 1959.——The **Mid-Central States Orthopaedic Society** has elected the following officers for 1958-1959: president, Dr. Werner P. Jensen, Omaha; vice-president, Dr. Harry O. Anderson, Wichita; past-president, Dr. Francis W. Carruthers, Little Rock; and secretary-treasurer, Dr. Henry O. Marsh, Wichita. The next meeting of the society will be held in Omaha about the first week in April, 1959.

Awards for Nutrition Essays.—Dr. Edgar F. Dunton and Dr. James R. Smith, of the University of Texas Medical Branch, Galveston, won the grand prize of $750 in the J. B. Roerig and Company's nationwide nutrition essay contest for medical students, interns, and resident physicians with their essay, "High Protein Feeding in the Severely Burned Patient." Three other prize winners each received $250; Jack William Hall, a junior student at Medical College of Virginia, Richmond, for "Nutritional Aspects of the Anemic State"; Vincent J. Fisher, a senior at New York State University College of Medicine, Brooklyn, for "Kwashiorkor, A Challenge in Preventive Medicine"; and Dr. J. Sidney Fulmer, an intern at Greenville General Hospital, Greenville, S. C., who won in the intern category for a paper on obesity, "The Pickwickian Syndrome—A Nutritional Disease." Contest judges were Dr. Robert S. Goodhart, scientific director, National Vitamin Foundation, New York; Dr. Robert E. Olson, head, department of biochemistry and nutrition, Graduate School of Public Health, University of Pittsburgh; and Max K. Horwitt, Ph.D., director of biochemical research, Elgin State Hospital, Elgin, Ill. J. B. Roerig and Company is a pharmaceutical division of Charles Pfizer and Company, Inc., New York City.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Oral Examination.* San Francisco, Sept. 29-Oct. 3, and Phoenix, April 5-10, 1959. The 1959 written examination will be given in various locations in the United States and Canada, July 17. The final date for filing application for the 1959 written examination is six months prior to the examination. There is no filing deadline for oral examinations. Sec., Dr. Curtiss B. Hickcox, 217 Farmington Ave., Hartford 8, Conn.

American Board of Dermatology: *Written. Several Cities,* June 30. *Oral.* Detroit, Oct. 17-19. Final date for filing all applications is April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Written.* Oct. 20, 1958. *Oral.* Philadelphia, April 23-26; San Francisco, June 18-21; Chicago, Oct. 13-16. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: Applications for certification, new and reopened, Part I, and requests for re-examination Part II, are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of application is September 1, 1958. No application can be accepted after that date. It should be noted by prospective candidates that the deadline date in 1959 is August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written,* qualifying test (Part I), January 1959. Final date for filing application is July 1, 1958. *Oral Examinations 1958* (Part II): San Francisco, June 17-21; Chicago, Oct. 17-22. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications is Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 6-10. Final date for filing application was April 30. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Chicago, Oct. 30-Nov. 1. Final date for filing application is Sept. 30. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Oral.* Chicago, Oct. 24-26 and New York, Dec. 5-7. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Plastic Surgery: *Oral and Written.* Chicago, Oct. 9-11. Final date for receipt of case reports is July 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

American Board of Proctology: *Oral and Written, Parts I and II.* September 1958. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Regular Examination in Radiology.* Washington, D. C., Dec. 8-12. Final date for filing application is July 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: Written examinations (Part I) will be held at various centers in the United States, Canada, Hawaii, Puerto Rico, and certain military centers abroad on December 3. The date of the Fall examination in *Part I* has been changed from the last Wednesday of October as announced in its current Booklet of Information to December 3, 1958. Thereafter, examinations in Part I will be held once annually, on the first Wednesday of December. The closing date for filing applications will be August 1. *Part II.* Baltimore, March 10-11. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: The fall written examination will be given in September 1958 and closing date for registration is July 1. Registration for the fall oral examination closes July 1.

American Board of Urology: *Written Examination.* Twenty-five cities throughout the country, Dec. 5. The oral will be given in Chicago in February 1959. Sec., Dr. William Niles, Wishard, Jr., 30 Westwood Road, Minneapolis 26.

DEATHS

Adamsons, Oscar Karlis Sr. ⊕ Staten Island, N. Y.; Universität Bern Medizinische Fakultät, Switzerland, 1914; interned at St. Vincent's Hospital and served a residency at the Sea View Hospital in Staten Island; associated with the department of correction in New York City; died in New York City April 29, aged 69, of carcinoma of the stomach.

Allen, Charles Insley Sr. ⊕ Wadesboro, N.C.; Columbia University College of Physicians and Surgeons, New York City, 1913; veteran of World War I; on the staff of the Anson County Hospital; president of the Bank of Wadesboro; died April 10, aged 67, of coronary occlusion.

Allen, Sylvia ⊕ Kansas City, Mo.; Columbia University College of Physicians and Surgeons, New York City, 1926; on the faculty of the University of Kansas School of Medicine, Kansas City, Kan.; member of the American Psychoanalytic Association and the American Psychiatric Association; formerly associated with Menninger Clinic in Topeka, Kan.; died in the Research Hospital April 15, aged 66, of heart disease.

Barkan, Otto ⊕ San Francisco; Ludwig-Maximilians-Universität Medizinische Fakultät, Munchen, Bavaria, Germany, 1914; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the Association for Research in Ophthalmology; served on the faculty of Stanford University School of Medicine; in 1954 the Section of Ophthalmology of the American Medical Association awarded him the Lucien Howe Medal for research in ophthalmology and allied branches; veteran of World War I; associated with St. Joseph's and Stanford University hospitals; died April 26, aged 71, of cerebral hemorrhage.

Bauer, Otto Michael ⊕ Forest Hills, N. Y.; Medizinische Fakultät der Universität, Vienna, Austria, 1919; died March 27, aged 64, of acute coronary occlusion, coronary arteriosclerotic heart disease, cerebral arteriosclerosis, and cerebral thrombosis.

Benner, Charles Russell ⊕ Chicago; Northwestern University Medical School, Chicago, 1905; on the staff of the Englewood Hospital, where he died April 29, aged 78, of carcinoma of the rectum with metastasis.

Blair, John Calvin, Kerens, Texas; University of Louisville (Ky.) Medical Department, 1892; died April 10, aged 90.

Brennan, Thomas Francis, Lowell, Mass.; Kansas City (Mo.) University of Physicians and Surgeons, 1929; died in St. John's Hospital April 10, aged 53.

Bryan, William Wright ⊕ Atlanta, Ga.; Emory University School of Medicine, Atlanta, 1932; clinical associate professor of radiology at his alma mater; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; vice-chairman, Section on Radiology, American Medical Association, 1957-1958; on the staffs of the Ponce de Leon Ear, Nose and Throat Infirmary and Grady Hospital; died April 10, aged 49, of a heart attack.

Carter, Donald Earl ⊕ Washington, D.C.; Atlanta College of Physicians and Surgeons, 1913; service member of the American Medical Association; during World War I served as a captain in Great Britain's Royal Army Medical Corps, and was decorated by King George V with the Military Cross; associated with the Veterans Administration; died in the George Washington University Hospital April 14, aged 63.

Case, Clarence E. ⊕ Ashtabula, Ohio; Western Reserve University Medical Department, Cleveland, 1895; fellow of the American College of Surgeons; medical examiner for the New York Central System for many years; associated with the Ashtabula General Hospital; a charter member and first president of the Ashtabula Rotary Club; died April 9, aged 87, of squamous-cell carcinoma of the hands.

Clough, William Plummer ⊕ New London, N.H.; Dartmouth Medical School, Hanover, 1911; veteran of World War I; for many years town health officer; on the staff of the New London Hospital, where he died April 9, aged 78.

Condon, Stanley ⊕ Detroit; Wayne University College of Medicine, Detroit, 1943; interned at Los Angeles County Hospital in Los Angeles; served a residency at Providence Hospital in Detroit; captain in the medical corps of the U. S. Air Force Reserve from June, 1953, to June, 1955; associated with St. John and Holy Cross hospitals; died April 5, aged 40, of a cardiovascular accident.

Dawkins, James Toliver, Birmingham, Ala.; University of Alabama School of Medicine, Mobile, 1909; served on the staffs of the Birmingham Baptist Hospital, West End Branch, and South Highlands Infirmary; died April 6, aged 76, of a heart attack.

⊕ Indicates Member of the American Medical Association.

DeLoatch, Mahlon Wingate, Tarboro, N. C.; Medical College of Virginia, Richmond, 1928; past-president of the Edgecombe-Nash Counties Medical Society; on the staff of the Edgecombe General Hospital, where he died April 12, aged 54, of coronary occlusion.

Doering, Valentine Theodore, Fort Madison, Iowa; St. Louis University School of Medicine, 1911; an associate member of the American Medical Association; served as city physician; on the staff of the Sacred Heart Hospital; died in St. Louis, April 1, aged 77, of pneumonia.

Drosin, Louis, New York City; Baltimore Medical College, 1905; member of the Medical Society of the State of New York; associated with the Beth David Hospital; died April 17, aged 76, of cerebral embolism.

Duff, John, La Jolla, Calif.; Tufts College Medical School, Boston, 1916; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; served in the regular Navy; for many years practiced in New York City, where he was clinical professor of urology at the New York Medical College, Flower and Fifth Avenue Hospitals and professor of urology, New York Polyclinic Medical School and Hospital, and was associated with the Morrisania Hospital; died in the Mercy Hospital in San Diego, April 20, aged 64, of bronchogenic carcinoma.

Dwyer, Christopher Edward ✠ Waterbury, Conn.; Georgetown University School of Medicine, Washington, D. C., 1925; past-president of the Waterbury Medical Society and of the New Haven County Medical Society; served as president of the board of health; veteran of World War II; on the staff of Waterbury Hospital, where he died April 18, aged 59, of hypertensive heart disease.

Ehlman, Frank H., Milwaukee, Wis.; Milwaukee Medical College, 1899; died in Pewaukee April 16, aged 86, of arteriosclerotic heart disease.

Files, Ernest Woodbury, Portland, Maine; Medical School of Maine, Portland, 1905; fellow of the American College of Surgeons; for many years chief of the gynecological service at the Maine General Hospital; associated with the Webber Hospital in Biddleford and the Mercy Hospital; died April 10, aged 76.

Goodman, James Edwards Jr., Bradenton, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1902; formerly practiced in Warrensburg, N.Y.; died Feb. 22, aged 86.

Grant, Iva Bouslough, Chicago; Kansas City (Mo.) Hahnemann Medical College, 1913; died in the Chicago Wesley Memorial Hospital April 17, aged 60, of acute myocardial infarction and arteriosclerotic heart disease.

Gunn, Milus Liddell ✠ Harlan, Ky.; University of Louisville School of Medicine, 1920; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the International College of Surgeons and the American College of Surgeons; consulting ophthalmologist of Louisville and Nashville Railroad Company; on the staffs of the Harlan Memorial and Harlan hospitals; died April 3, aged 61, of acute myocardial infarction and coronary occlusion.

Hare, Milton Metcalfe, Saratoga, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1925; died in San Jose April 6, aged 73.

Hauser, Charles David, Youngstown, Ohio; University of Buffalo School of Medicine, 1896; past- president of the Mahoning County Medical Society and president of the Sixth Councilor District Assembly in 1921; fellow of the American College of Surgeons; veteran of World War I; associated with St. Elizabeth Hospital, where he died April 7, aged 82.

Hodgdon, Ola Wilfred, Franklin, N.H.; Boston University School of Medicine, 1904; died in the Franklin Hospital April 5, aged 82, of arteriosclerotic heart disease and uremia.

Holleran, James Francis, Los Angeles; University of Southern California College of Medicine, Los Angeles, 1908; member of the American Academy of General Practice; served on the faculty of College of Medical Evangelists; associated with the Queen of Angels Hospital; died April 10, aged 72, of old myocardial infarctions and arteriosclerosis.

Hopkins, Percy Isaiah ✠ Dothan, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1899; fellow of the American College of Surgeons; associated with Moody and Frasier Ellis hospitals; died April 4, aged 78.

Houck, George E. ✠ Roseburg, Ore.; University of Oregon Medical School, Portland, 1890; past-president of the Southern Oregon Medical Society; fellow of the American College of Surgeons; formerly member of the city council, mayor and city and county health officer; served in France during World War I; at one time member and president of the state board of health; associated with the Mercy Hospital; died in Portland April 14, aged 92.

DEATHS

Adamsons, Oscar Karlis Sr. ⊕ Staten Island, N. Y.; Universität Bern Medizinische Fakultät, Switzerland, 1914; interned at St. Vincent's Hospital and served a residency at the Sea View Hospital in Staten Island; associated with the department of correction in New York City; died in New York City April 29, aged 69, of carcinoma of the stomach.

Allen, Charles Insley Sr. ⊕ Wadesboro, N.C.; Columbia University College of Physicians and Surgeons, New York City, 1913; veteran of World War I; on the staff of the Anson County Hospital; president of the Bank of Wadesboro; died April 10, aged 67, of coronary occlusion.

Allen, Sylvia ⊕ Kansas City, Mo.; Columbia University College of Physicians and Surgeons, New York City, 1926; on the faculty of the University of Kansas School of Medicine, Kansas City, Kan.; member of the American Psychoanalytic Association and the American Psychiatric Association; formerly associated with Menninger Clinic in Topeka, Kan.; died in the Research Hospital April 15, aged 66, of heart disease.

Barkan, Otto ⊕ San Francisco; Ludwig-Maximilians-Universität Medizinische Fakultät, Munchen, Bavaria, Germany, 1914; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the Association for Research in Ophthalmology; served on the faculty of Stanford University School of Medicine; in 1954 the Section of Ophthalmology of the American Medical Association awarded him the Lucien Howe Medal for research in ophthalmology and allied branches; veteran of World War I; associated with St. Joseph's and Stanford University hospitals; died April 26, aged 71, of cerebral hemorrhage.

Bauer, Otto Michael ⊕ Forest Hills, N. Y.; Medizinische Fakultät der Universität, Vienna, Austria, 1919; died March 27, aged 64, of acute coronary occlusion, coronary arteriosclerotic heart disease, cerebral arteriosclerosis, and cerebral thrombosis.

Benner, Charles Russell ⊕ Chicago; Northwestern University Medical School, Chicago, 1905; on the staff of the Englewood Hospital, where he died April 29, aged 78, of carcinoma of the rectum with metastasis.

Blair, John Calvin, Kerens, Texas; University of Louisville (Ky.) Medical Department, 1892; died April 10, aged 90.

Brennan, Thomas Francis, Lowell, Mass.; Kansas City (Mo.) University of Physicians and Surgeons, 1929; died in St. John's Hospital April 10, aged 53.

Bryan, William Wright ⊕ Atlanta, Ga.; Emory University School of Medicine, Atlanta, 1932; clinical associate professor of radiology at his alma mater; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; vice-chairman, Section on Radiology, American Medical Association, 1957-1958; on the staffs of the Ponce de Leon Ear, Nose and Throat Infirmary and Grady Hospital; died April 10, aged 49, of a heart attack.

Carter, Donald Earl ⊕ Washington, D.C.; Atlanta College of Physicians and Surgeons, 1913; service member of the American Medical Association; during World War I served as a captain in Great Britain's Royal Army Medical Corps, and was decorated by King George V with the Military Cross; associated with the Veterans Administration; died in the George Washington University Hospital April 14, aged 63.

Case, Clarence E. ⊕ Ashtabula, Ohio; Western Reserve University Medical Department, Cleveland, 1895; fellow of the American College of Surgeons; medical examiner for the New York Central System for many years; associated with the Ashtabula General Hospital; a charter member and first president of the Ashtabula Rotary Club; died April 9, aged 87, of squamous-cell carcinoma of the hands.

Clough, William Plummer ⊕ New London, N.H.; Dartmouth Medical School, Hanover, 1911; veteran of World War I; for many years town health officer; on the staff of the New London Hospital, where he died April 9, aged 78.

Condon, Stanley ⊕ Detroit; Wayne University College of Medicine, Detroit, 1943; interned at Los Angeles County Hospital in Los Angeles; served a residency at Providence Hospital in Detroit; captain in the medical corps of the U. S. Air Force Reserve from June, 1953, to June, 1955; associated with St. John and Holy Cross hospitals; died April 5, aged 40, of a cardiovascular accident.

Dawkins, James Toliver, Birmingham, Ala.; University of Alabama School of Medicine, Mobile, 1909; served on the staffs of the Birmingham Baptist Hospital, West End Branch, and South Highlands Infirmary; died April 6, aged 76, of a heart attack.

⊕ Indicates Member of the American Medical Association.

tration Hospital in Metuchen and the Muhlenberg Hospital in Plainfield; died April 10, aged 62, of cerebral hemorrhage.

Munk, Cleoric Erwin ✠ Kendallville, Ind.; Eclectic Medical College, Cincinnati, 1912; served as president of the Northeastern Indiana Academy of Medicine; died in the McCray Memorial Hospital April 4, aged 73.

Murphy, John Campbell ✠ Aurora, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; veteran of World War I; associated with St. Joseph and Copley hospitals, and St. Charles Hospital, where he died April 9, aged 82, of bronchopneumonia, arteriosclerotic heart disease, and bleeding peptic ulcer.

Mussey, Robert Daniel ✠ Rochester, Minn.; born in Glendale, Ohio, Jan. 10, 1884; Medical College of Ohio. Cincinnati, 1908; emeritus professor of obstetrics and gynecology at the University of Minnesota Graduate School; for many years a member of the staff of the Mayo Clinic, where he became a member of the board of governors in 1933 and in 1937 was named board chairman; during World War I served as a captain, and then major, in the medical corps of the U. S. Army; specialist certified by the American Board of Obstetrics and Gynecology and served as a director of that board; president of the Minnesota Society of Obstetrics and Gynecology in 1937, the American Association of Obstetricians and Gynecologists in 1948, and the Central Association of Obstetricians and Gynecologists in 1938; member of the American Gynecological Society, Minnesota Academy of Medicine, the Society of the Sigma Xi, Alpha Omega Alpha and the Alumni Association of the Mayo Foundation; in 1937 chairman of the Minnesota Committee on Maternal Welfare; served as director of the American Committee on Maternal Welfare; for many years on the staff of St. Mary's Hospital, where he died April 20, aged 74, of cardiovascular accident.

Nachlas, I. William ✠ Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1918; associate professor of orthopedic surgery at his alma mater; specialist certified by the American Board of Orthopaedic Surgery; member of the American Orthopaedic Association and the American Academy of Orthopaedic Surgeons; veteran of World Wars I and II; served on the staffs of Sinai, Mount Pleasant, Provident, Union Memorial, Women's, and West Baltimore General hospitals, and the Children's Hospital School; member of the American board of associate editors of the *Journal of Bone and Joint Surgery;* died in Johns Hopkins Hospital April 20, aged 63.

Natter, Alexander L., Woodside, N. Y.; Long Island College Hospital, Brooklyn, 1923; died in the Kew Gardens (N. Y.) General Hospital March 13, aged 60, of acute posterior-wall infarction and arteriosclerotic heart disease.

Nemirow, Martin, Passaic, N. J.; Eclectic Medical College of the City of New York, 1911; died in the St. Mary's Hospital, Passaic, April 17, aged 77.

Paley, Samuel Morris, New York City; University and Bellevue Hospital Medical College, New York City, 1921; member of the Medical Society of the State of New York; specialist certified by the American Board of Physical Medicine and Rehabilitation; veteran of World Wars I and II; formerly associated with the U. S. Public Health Service; died in the Veterans Administration Hospital March 25, aged 59, of bronchopneumonia, cardiovascular accident, and arteriosclerosis.

Paul, James Richard ✠ North Hollywood, Calif.; University of Nebraska College of Medicine, Omaha, 1942; veteran of World War II; member of the American Psychiatric Association; resigned from the regular U.S. Army Oct. 29, 1946; died March 28, aged 42, of bronchopneumonia.

Pogue, Richard Ewart ✠ Carson City, Nevada; College of Medical Evangelists, Loma Linda and Los Angeles, 1933; served as superintendent of the Cottage Hospital in Watertown, Minn., and on the staffs of the Fairview and Swedish hospitals in Minneapolis; died Feb. 22, aged 52, of chronic rheumatic heart disease.

Powell, Annie Monica Dunn, Louisville, Ky.; University of Bombay, India, 1892; formerly a medical missionary; died in the Jewish Hospital March 19, aged 88.

Power, Younger Lovelace ✠ Ilion, N. Y.; Medical College of Virginia, Richmond, 1932; served as mayor of Ilion; on the staff of the Ilion Hospital; died March 4, aged 51, of coronary heart disease.

Rake, Geoffrey William, New York City; born in Fordingbridge, England, Oct. 18, 1904; L. R. C. P., London and M. R. C. S., England, 1927; after serving at Guy's Hospital in London, joined the teaching staff of Johns Hopkins Hospital in Baltimore; later became a member of the research staff of the Rockefeller Institute for Medical Research, and spent a year as research associate in the Connaught Laboratories, University of Toronto; joined Squibb in 1937 as head of the microbiology division of the Squibb Institute for Medical Research, in New Brunswick, N. J., of which he became director; became medical research consultant to the E. R. Squibb & Sons Division of Olin Mathieson Chemical Corpora and director of the Squibb medical division; in 1956 named scientific director of the International division of Olin Mathieson Chemical Corporation; recipient of the Gold Medal in Medicine of the University of London; one of the original members of the virus and rickettsial study section and the syphilis study section of the U. S. Public Health Service; member of the Society of American Bacteriologists, Society for Experimental Biology and Medicine, American Society of Epidemiologists, American Association of Immunologists, Harvey Society, New York Academy of Medicine, and the Royal Society of Medicine; fellow of the American College of Physicians; served as mayor of Millstone, N. J.; in 1953 joined the staff of the University of Pennsylvania schools of medicine and veterinary medicine in Philadelphia, where he served as a member of the Wistar Institute of Anatomy and Biology; known for his research in virus diseases and tuberculosis; joint author with Dr. Harvey Blank, "Viral and Rickettsial Diseases of the Skin, Eye and Mucous Membranes of Man"; a contributor to scientific textbooks; died in the Princeton (N. J.) Hospital April 20, aged 53.

Rosenstein, Isaac, New York City; University and Bellevue Hospital Medical College, New York City, 1908; died March 28, aged 72, of cerebral thrombosis and arteriosclerosis.

Rosenzweig, Joseph, Brooklyn; New York Homeopathic Medical College and Flower Hospital, New York City, 1933; member of the Medical Society of the State of New York; veteran of World War II; died March 20, aged 49, of coronary thrombosis and hypertension.

Seaman, Charles LeRoy ⊕ Cherokee, Iowa; Creighton University School of Medicine, Omaha, 1935; veteran of World War II; formerly city health officer; district surgeon for the Illinois Central Railroad; died April 5, aged 50, of acute coronary occlusion.

Silsby, Frederick Ward, Atlanta, Ga.; Western Pennsylvania Medical College, Pittsburgh, 1905; an associate member of the American Medical Association; member of the Medical Society of the State of Pennsylvania and the American Academy of Dermatology and Syphilology; formerly practiced in Tarentum, where he was associated with the Allegheny Valley Hospital; died April 8, aged 85, of coronary thrombosis, chronic nephritis, and diabetes mellitus.

Slay, Iris Joe, Purvis, Miss.; Memphis (Tenn.) Hospital Medical College, 1913; veteran of World Wars I and II; died April 20, aged 70 of coronary thrombosis.

Smith, Chandler White ⊕ Captain, U.S. Navy, retired, Washington, D.C.; born in Urbana, Ohio, March 11, 1883; Hahnemann Medical College and Hospital of Philadelphia, 1907; commissioned in the medical corps of the U.S. Navy in 1908 as an assistant surgeon with the rank of lieutenant (jg); served on continuous active duty with the Navy Medical Department until he was placed on the retired list of Naval Officers on June 30, 1936; attained the rank of commander in 1925; recalled to active duty in a retired status in October, 1939, and served until 1946, attaining the rank of captain in 1943; during his more than 35 years active Naval service, served with the Medical Department of the Navy throughout the United States and abroad, and in ships of the fleet; at the time of his release to inactive duty in 1946 was serving on duty at the National Naval Medical Center in Bethesda, Md.; died in the U.S. Naval Hospital in Bethesda April 9, aged 75.

Spain, Robert Thomas ⊕ Conrad, Iowa; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; served on the staff of the Evangelical Deaconess Home and Hospital in Marshalltown; died April 1, aged 82, of heart disease.

Stanford, James Willingham ⊕ Cartersville, Ga.; Medical College of Georgia, Augusta, 1928; president of the Bartow County Medical Society; died Feb. 24, aged 56, of uremia, pyelonephrosis, and nephrolithiasis.

Strange, Shelby Phipps ⊕ San Francisco; Cooper Medical College, San Francisco, 1912; for many years associated with the Southern Pacific General Hospital; died April 6, aged 82.

Stratte, John Joseph Jr., Modesto, Calif.; Rush Medical College, Chicago, 1942; served on the staffs of the San Joaquin Hospital in Bakersfield, Bret Harte Sanatorium in Murphys, and the DeWitt State Hospital in Auburn; died April 12, aged 44, of injuries received in an automobile accident.

Taylor, Walter Oglethorpe, Boston; College of Physicians and Surgeons, Boston, 1909; died April 3, aged 81.

Thigpen, Charles Alston ⊕ Montgomery, Ala.; born in Greenville, Ala., Dec. 19, 1865; Medical Department of Tulane University of Louisiana, New Orleans, 1888; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; past-president of the Medical Association of the State of Alabama; member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological, Rhinological and Otological Society, and the Association for Research in Ophthalmology; fellow of the American College of Surgeons; in 1916 member of the House of Delegates of the American Medical Association; veteran of World War I; served on the staff of St. Margaret's Hospital; died April 23, aged 92, of heart disease.

Tucker, Gabriel, Rosemont, Pa.; born in Wheeling, W. Va., Nov. 3, 1880; Jefferson Medical College of Philadelphia, 1905; emeritus professor of bronchoscopy, esophagology, and laryngology surgery at the University of Pennsylvania Graduate School of Medicine and served as professor of bronchoscopy and esophagology at the University of Pennsylvania School of Medicine in Philadelphia; specialist certified by the American Board of Otolaryngology; an associate member of the American Medical Association and at one time secretary and chairman of its Section on Laryngology, Otology and Rhinology; member of the American Association of Thoracic Surgery, American Academy of Ophthalmology and Otolaryngology and was elected to its honor society, American Laryngological Association, American Laryngological, Rhinological and Otological Society, and the American Broncho-Esophagological Association, of which he was past-president; fellow of the American College of Surgeons; served overseas during World War I; formerly on the staff of the Graduate Hospital of the University of Pennsylvania where he was in charge of the Chevalier Jackson Bronchoscopic Clinic; associated with Misericordia Hospital, Bryn Mawr (Pa.) Hospital, Fitzgerald-Mercy Hospital in Darby, Abington (Pa.) Memorial Hospital, Children's Hospital, Jeanes Hospital, and the Germantown Dispensary and Hospital; died April 17, aged 77, of cardiac disease.

Twitchell, Benjamin E. ✠ Belleville, Ill.; American Medical College, St. Louis, 1891; past-president of the St. Clair County Medical Society; served as president of the U.S. Board of Pension Examiners, county physician and coroner of St. Clair County; on the staff of St. Elizabeth's Hospital; died April 14, aged 91, of arteriosclerotic heart disease.

Wallace, Henry, New York City; Long Island College *Hospital, Brooklyn, 1890; an associate member* of the American Medical Association; fellow of the American College of Physicians; veteran of the Spanish-American War; formerly on the staff of the Mountainside Hospital in Montclair, N. J.; died April 24, aged 89.

Warta, Joseph J., Omaha; John A. Creighton Medical College, Omaha, 1902; associate professor of ophthalmology at his alma mater; associated with St. Joseph's Hospital; died April 14, aged 81, of acute myocardial infarction.

Wassell, Corydon McAlmont, Little Rock, Ark.; born in 1883; University of Arkansas School of Medicine, Little Rock, 1909; for many years a medical missionary in China; at one time health officer of Pulaski County; commissioned as a lieutenant commander in the medical corps of the U. S. Naval Reserve in 1940; assigned to caring for wounded officers and men of the cruisers Houston and Marblehead; commended by the late President Roosevelt in his radio address on April 28, 1942, for heroism in Java; awarded the navy cross for evacuating 12 badly wounded American servicemen under heavy Japanese gunfire in Java; refusing to leave the men to certain capture, he evacuated them on March 1, 1942, under heavy fire from both aircraft and ground troops; retired as a rear admiral; his heroism during World War II was the theme of a novel and motion picture; died May 12, aged 74.

Watkins, J. Frank, Temple City, Calif.; University of Tennessee College of Medicine, Memphis, 1919; served on the staffs of the Behrens Memorial Hospital in Glendale and the French Hospital in Los Angeles; died in Covina March 22, aged 69, of a heart attack.

Whigham, Arthur Lee, Newville, Ala.; University of Alabama School of Medicine, Mobile, 1910; died April 4, aged 70, of rupture of abdominal aneurysm.

Williams, Angus S. ✠ Renton, Wash.; Medico-Chirurgical College of Philadelphia, 1899; member of the American Academy of General Practice; died in the Virginia Mason Hospital April 16, aged 87, of bronchopneumonia.

Williams, Gordon Darnall ✠ Weatherford, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1927; veteran of World War II; died April 1, aged 57.

Winn, William M. Jr. ✠ Clarksville, Va.; Medical College of Virginia, Richmond, 1911; died in Atlantic City, N.J., April 20, aged 69, of acute myocardial infarction.

Worth, Charles Mansfield ✠ Denver; Denver College of Physicians and Surgeons, 1907; died April 15, aged 89, of carcinoma of the throat with metastasis and arteriosclerosis.

Wotherspoon, Gordon ✠ Seattle; University of Glasgow Medical Faculty, Scotland, 1934; veteran of World War II; died April 19, aged 53.

Young, Edward Bradley, Zachary, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1896; an associate member of the American Medical Association; died March 11, aged 86, of cardiac failure and cerebral accident.

FOREIGN LETTERS

AUSTRIA

Air Gun Injuries.—At the meeting of the Society of Physicians in Vienna on May 2, Dr. A. Gund reported on suicides committed with the aid of an air gun designed to render animals unconscious before slaughtering. The gun is placed directly against the head. In penetrating the cranium a bone chip of the caliber of the cartridge is punched out by the nose of the cartridge. The bone chip acting as secondary projectile is driven into the brain. The injury is fatal if the bone chip reaches the area of the third ventricle. Of two patients reported on one survived after an intracranial operation because the bone chip passed along the anterior base of the skull toward the posterior nares.

Inoculation Metastasis.—At the same meeting Dr. J. Glaninger said that the production of inoculation metastasis depends on the viability of the transmitted cells and the nature or susceptibility of the new bed. These factors are present when, for the purpose of resection of a carcinoma of the larynx, anesthesia is induced by peroral intubation. The consistency of the tracheal catheter and the slight pressure used with intubation are such that viable cells may be separated from the cancer and displaced into the lung. This applies especially if the tube must be forced past a stenotic area; otherwise the dissemination is hematogenous or lymphogenous.

Human Milk Center.—At the meeting of the Society of Pediatrics in April Dr. H. O. Juergenssen said that human milk represents the optimal food for the nursing infant and is an absolute necessity in feeding premature infants, dystrophic infants, and those with severe nutritional disturbances. The human milk center collects the surplus of milk from hypergalactic women, since wet-nurses are a thing of the past. Nurses, who have at their disposal small buses provided with cooling apparatus, collect the milk from the donors (about 2,000 per year) and from maternity wards daily. On the average nearly 1,000 liters are collected per month. As soon as the milk arrives at the center, it is examined for possible adulteration, acidity, and impurities. It is boiled for five minutes and then refrigerated. It is distributed only on prescription. The price is about $1.40 per liter. Because the supply sometimes exceeds the demand, various methods of preservation have been tried. Lyophilization is the only method which preserves the raw character of the milk and such thermolabile constituents as enzymes, inhibins, and vitamins. Once lyophilized, the milk can be stored at room temperature indefinitely, and requires little storage space.

Pulmonary Arteriovenous Aneurysm.—At the meeting of the Society of Physicians in Vienna on May 9, Dr. Wenzl stated that pulmonary arteriovenous aneurysm is an embryonal malformation in the pulmonary circulation, resulting in a right-to-left shunt. An operation is necessary because of the high mortality resulting from rupture of the aneurysm and cerebral complications. In the course of the operation the arterial oxygen saturation may be tested to determine the success of the operation. If reduction of the flow through the arterial branches that lead to the aneurysm results in normalization of the decreased arterial oxygen saturation, proof is provided that the shortcut circulation is completely interrupted. Extracardiac as well as cardiac causes may be responsible for the genesis of congenital cyanosis.

Dr. F. Schmidt said that an important factor in the production of central cyanosis and symptomatic polycythemia is the decreased oxygen content of the arterial blood. Hypoxemia frequently occurs in pulmonary diseases. The mechanisms leading to that occurrence can be determined by a combined examination of pulmonary function. The examination is performed with the aid of a spirometric ventilation test and an analysis of the arterial blood. The analysis of the arterial blood is performed during rest, after oxygen inhalation for at least 10 minutes, and during exercises with the ergometer bicycle. An insignificant influence on the arterial hypoxemia during oxygen inhalation is considered proof of a left-to-right shunt of at least 15% of the minute-time volume of the heart. Cyanosis is not manifested when anemia is present at the same time. Other mechanisms that lead to arterial hypoxemia, polycythemia, and cyanosis include the chronically deficient oxygen supply of the lung associated with chronic, spastic bronchitis and the "disturbance of diffusion" (alveolocapillary block) shown in patients with diffuse pulmonary fibrosis. Dr. H. Ellegast stated that roentgenography is an important factor in the diagnosis of pulmonary arteriovenous aneurysm. Single aneurysms present a particular roentgenographic and diagnostic problem. A more or less pronounced change in size of this vascular tumor is revealed by the Valsalva and

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The items in these letters are contributed by regular correspondents in the various foreign countries.

Mueller tests. Pulsations can be defined by means of a kymogram. With the use of tomography, which should be carried out on two planes, it is usually possible to show the relationship of a shadow, which at first may have an atypical appearance with dilated afferent and efferent vessels.

Tuberculosis and Pregnancy.—At the same meeting Dr. Jentgens stated that statistics show that (1) pregnancy does not interefere with the treatment of tuberculosis, (2) the success of the treatment of tuberculosis during pregnancy depends on the understanding and full cooperation of the patient, and (3) the early detection of all persons with tuberculosis is important to the success of treatment. The family physician should advise his pregnant patients as to signs of tuberculosis. Fifty-one patients with extrapulmonary tuberculosis, including some with recent tuberculous spondylitis which required operation, were treated during pregnancy. In one patient nephrectomy had to be performed during pregnancy. All methods of treatment are applicable to pregnant patients with pulmonary tuberculosis. The same applies to chemotherapy and treatment by resection. No difference is made between the treatment of pregnant and nonpregnant patients. In a series of 21 pulmonary resections performed during pregnancy, all operations led to obliteration of the cavities and conversion of the sputum to negative. Birth and confinement were without complications in those patients. With modern method of treatment interruption of pregnancy because of tuberculosis is no longer indicated. After delivery the treatment for tuberculosis may have to be continued for several months. Operation if required should not be performed until two to three months after delivery.

CANADA

Talar Fusions.—Mustard and Laurin (*Canad. J. Surg.* 1:201, 1958) reviewed a series of 301 patients with fusions about the ankle and foot in children. They had good results in 73 to 90%, depending on the operation used. They found that the extra-articular subtalar fusion described by Grice was easily and safely obtained in patients 5 years of age. It was performed to maintain subtalar alignment and stability after correction of a valgus or varus deformity. It could be performed earlier if it was desired to discard a brace. After 8 years of age, it was best to defer fusion until a triple arthrodesis could be performed in patients at the age of 12. In the latter operation, internal fixation with staples was found useful and correction of muscle imbalance essential. A Lambrinudi fusion was found to provide good correction of idiopathic talipes cavus without sacrifice of length, but it should not be done for a paralytic talipes cavus. It provided good correction of dynamic and fixed talipes equinus after poliomyelitis or cerebral palsy. Ankle fusions alone were rarely indicated for paralysis in children. If necessary they can be performed by the Gallie technique without disturbing growth. For children with flail legs below the knees, patellar arthrodeses gave excellent results but were inadequate if the hips were unstable.

Radiation Hazards.—Johns and Wilson; (*Canad. M. A. J.* 78:571, 1958) investigated the gonadal dose of radiation received by persons in the mass chest roentgenography program in Ontario. They used paraffin wax phantoms with an ion chamber centered at a point representing the average position of the ovaries. A number of experiments indicated that the female gonadal dose received depended almost entirely on the distance from the iliac crest to the lower edge of the x-ray beam. It is therefore essential to know the exact location of the lower edge of the beam on each unit used. This was determined by the use of films and lead strips. In all units tested, the beam was found to extend below the screen. The investigators concluded that the gonadal dose may be reduced by (1) replacing all circular cones with rectangular cones and inserts; (2) ensuring that the beam does not extend below the screen; (3) placing the subject with the iliac crest as far below the screen edge as possible; and (4) increasing the speed of the camera screen and film and avoiding overexposure and underdevelopment. Use of a filter had little effect on the gonadal dose. These precautions have now been applied to all miniature film units in Ontario, and it has become evident that with them the gonadal dose from mass roentgenography of the chest may be reduced to 0.26 mr or 0.25% of the background irradiation, where it is probably not a significant hazard. Use of faster films when they become available will probably reduce the dose by a further factor of 2.

Myocardial Revascularization.—For several years, Vineberg and co-workers have treated coronary artery insufficiency by implantation of the internal mammary artery into the myocardium. They have had excellent results from this, but the method has its limitations, and they have therefore constantly searched for other methods of myocardial revascularization. Recently they reported on the use of Ivalon sponge application to the bared myocardium in animals in whom coronary insufficiency was induced by application of ameroid constrictors around the coronary vessels. Most control animals died within 27 days of myocardial ischemia, but all of 14 animals to whose myocardium the sheets of Ivalon sponge were applied lived well beyond the control series period, 11 of 14 being sacrificed two and a half to four months after operation. This time, in spite of the constriction of the coronary

1950. Operation is contraindicated in acute fulminating, hypertensive, and glycosuric forms of the disease. In those with the psychic forms or in whom ocular disturbances are predominant the treatment in each case must be decided on its merits. The three major indications for thyroidectomy are the forms with goiter, those refractory to medical treatment, and those accompanied by cardiac disturbances.

Mitral Stenosis.—J. Ducuing and co-workers (*Presse méd.* 66:654, 1958) reviewed a series of 100 operations for mitral stenosis. In 40 patients the operation was performed by use of the finger alone; in 55 patients who had stenosis with thickening of the valve the operation was performed by using Dubost's dilator, and in 5 patients with funnel-like stenosis, in whom the valve had been completely destroyed, nothing could be done. In this series five patients died. One patient died during operation when the pulmonary artery was injured by the point of the auricular clamp, one after two operations because of injury to the left ventricle caused by the heel of the clamp, one after reoperation and tracheotomy because of pulmonary edema, and two because of thrombosis or embolism. Several accidents occurred during the operations. These included seven lacerations of the atrium, two ventricular fibrillations (both patients recovered), and one embolism of the posterior tibial artery. The results in 75% of the patients were considered excellent.

ICELAND

Iceland's Health.—The official health report for 1954, published in 1957, shows a record low death-rate, with only 1,064 deaths in a population of 156,033 (6.9 per 1,000) 39.8% of whom live in the capital. As causes of death, heart disease came first with 250 cases, followed by cancer with 198, and cerebral apoplexy with 156. There were 7 deaths among the 6,573 patients with measles and 2 among the 2,076 patients with pertussis. None of the 11 cases of poliomyelitis proved fatal. The 476 cases of gonorrhea marked a sharp rise in incidence, but there was no new case of syphilis. Diphtheria was conspicuous by its absence, and only one case of puerperal fever was reported in the past five years. In the capital, 82.5% of the confinements occurred in hospital, and more than 25% of the babies were born out of wedlock. There was no typhoid in 1954, but paratyphoid yielded a crop of 111 cases in addition to 41 carriers of Salmonella paratyphi B. This epidemic caused no deaths. The university performed 240 autopies, 64 for medico-legal reasons.

INDIA

Influenza in Children.—P. M. Udani (*Indian J. Child Health* 7:4 [April] 1958) reported a series of 251 children with influenza observed in the pandemic in Bombay in May and June, 1957. The evidence that the illness in these children was due to an influenza virus was only circumstantial and epidemiological. It was hard to prove the diagnosis because of difficulties in isolating the virus and in carrying out serologic tests. The largest number of patients were seen in the first three weeks of the epidemic. No age was exempt, although the number of those under 3 months of age was relatively small. The youngest baby was 6 days old. He had fever and convulsions of one day's duration and died within a few hours of admission. Autopsy revealed typical lesions of influenza in the lungs. Another newborn baby had a temperature of 105 F (40.6 C) on the second day of life and died. His mother had influenza when he was born. There were 79 patients in the age group of 6 months to 3 years. In 156 of the children the disease was mild or moderately severe, and in 95 it was severe with complications; 12 of these had fulminating attacks and died in 3 or 4 days. Autopsy of these patients showed severe viral infection without secondary bacterial infection. The clinical findings were varied; 156 had an acute febrile attack with a sudden onset, and in 2 or 3 days in the moderately severe cases the findings resembled those of typhoid. Fifty-eight patients had the respiratory type of influenza. The upper respiratory tract was involved in most of them, but the lower respiratory tract was involved in all of these patients; 4 had tracheitis, 28 bronchitis, 21 bronchopneumonia and bronchiolitis, 2 bronchitis with pleuropneumonitis, 8 lobular pneumonia, 2 hemorrhagic pleurisy, and 10 predominantly interstitial pneumonia.

To what extent the lower respiratory lesions were due to the virus, or whether a superimposed bacterial infection caused these lesions, was difficult to say. In the 12 patients with fulminating attack there was no postmortem evidence of bacterial infection; pyogenic exudate was absent; and culture of the heart's blood was negative. In some who recovered, however, there was quick improvement with antibiotics, suggesting that bacterial infection played a secondary role. Fluoroscopy was performed on all patients and showed increased vascularity of the lungs and hilar regions in about 40%. Marked emphysema was seen in 50 patients; 8 had areas of pneumonitis; 2 had a small pleural effusion; 1 had pleurisy; and 1 had a patch of pleuropneumonia at the base of the lung. Nine had myocarditis with marked tachycardia, muffling of heart sounds, gallop rhythm, and an enlarged heart. One patient developed severe congestive cardiac failure and recovered within three weeks; five with myocarditis died. In three of these autopsy revealed petechial hemorrhages in the pericardium and myocardium.

The condition of five patients with persistent vomiting was classified as gastric influenza; three of these later developed severe dehydration and encephalopathy, and two had diarrhea with dehydration. Both of the patients with diarrhea died in shock, and autopsy revealed typical pulmonary lesions—one had intestinal ulcerations. Five patients had hematemesis at the onset in association with other clinical features of the disease. One had a frank intestinal hemorrhage. One of these five died. Twelve patients had severe abdominal pain with gastrointestinal symptoms. One of these died and on autopsy showed marked enlargement of the mesenteric lymph nodes, with typical pulmonary lesions. A laparotomy was performed on another patient whose disease started as typical influenza. He later developed severe abdominal pain with signs of subacute intestinal obstruction; the mesenteric lymph nodes were acutely inflamed, and there were peritoneal adhesions. Twenty-four patients had findings suggestive of meningoencephalitis; 11 of these died. Polyneuritis was seen in one patient who was admitted in a semiconscious state with convulsions, pharyngeal congestion, and bronchitic, but no meningeal, signs. His calf muscles were tender on pressure and weak. The deep reflexes were diminished in all four limbs. Some patients with influenza in other members of the family had palatal weakness on one side with an influenzal onset. Lumbar puncture, performed on 23 patients, gave clear fluid under increased pressure. The spinal fluid proteins were increased in 7; sugar was slightly diminished in 2 and increased in 4; and 7 showed pleocytosis, predominantly lymphocytic. No organisms were isolated from the spinal fluid.

Three patients developed diabetes insipidus in the course of the disease; six had hyperpyrexia and all of these died; two had subnormal temperature and died in shock. Autopsy of these showed the findings of influenza. In nearly 200 patients the fever lasted 2 to 7 days; in 19 it lasted 8 to 14 days; and 21 had fever varying from two weeks to five months in duration. Hemorrhage occurred in 10 patients (severe epistaxis in 3, hematemesis in 5, severe internal bleeding in 1, and petechiae in 1). One had hemorrhagic mucus in the throat at autopsy. Some children developed a measle-like rash. Hepatitis and jaundice was seen in others. Postinfluenzal syndromes included frequent respiratory infections, malnutrition with recurrent respiratory infection and recurrent gastrointestinal upset, flare-up of an old tuberculous lesion, severe anemia, exhaustion, and mental retardation (especially in those with meningoencephalitis). The highest mortality occurred in the youngest infants. Although the patients were classified clinically in different groups according to the system involved predominantly, the children usually had multiple lesions. Thus children with meningoencephalitis also had severe pulmonary lesions. In spite of the varied clinical findings, severe hemorrhagic, interstitial bronchopneumonia was the most striking finding at autopsy.

ISRAEL

Vitamin B_{12} Determination.—Rachmilewitz and Stein (*Harefuah* 54:169, 1958) stated that for the diagnosis of anemias and diseases of the liver, the determination of vitamin B_{12} in body fluids is of great value. Low serum vitamin B_{12} concentrations may be due to lack of intrinsic factor in the stomach, as in pernicious anemia and after gastrectomy. Disturbances in the absorption of vitamin B_{12} by the small intestine as in sprue, diverticulosis, or blind intestinal loops may also lead to vitamin B_{12} deficiency with low serum levels. Low vitamin B_{12} concentrations are also found in patients suffering from chronic malnutrition, low intake of vitamin B_{12}, and the anemia of pregnancy. A gradual decrease in serum vitamin B_{12} concentration precedes the development of anemia and the appearance of the characteristic morphologic changes in the bone marrow and peripheral blood. Megaloblastic anemia may be corrected by various means (folic acid or steroid hormones), but the vitamin B_{12} deficiency remains.

High serum vitamin B_{12} concentrations are found in viral and toxic hepatitis, the active stage of cirrhosis of the liver, chronic hepatic congestion due to heart failure, and malignant tumors invading the liver. Most of the serum vitamin B_{12} in patients with liver disease is bound to serum proteins, and the capacity of these proteins to bind vitamin B_{12} is increased. The increase of the vitamin B_{12} in the serum in liver disease is due to release of the stored vitamin from damaged liver cells. Since normal values of serum vitamin B_{12} are found in jaundice due to intrahepatic or extrahepatic obstruction, serum vitamin B_{12} determinations are helpful in differentiating hepatocellular from extrahepatic jaundice. In patients with liver disease and high serum vitamin B_{12} levels, the urinary excretion of the vitamin is increased. High serum vitamin B_{12} concentrations are found in myeloid leukemia but not in stem-cell leukemia or lymphocytic leukemia. All the vitamin B_{12} in the serum of patients with granulocytic leukemia is bound to protein. The urinary excretion of the vitamin in this disease is normal or below normal.

Rheumatic Fever Control.—Kagan and Brand (*Quart. Review "Harefuah"* 1:10, 1958) reported that rheumatic fever annually afflicts 2,500 persons, mostly children, in Israel, and almost invariably damages the heart. The national incidence of the disease is 1.5 per 1,000, but in Jerusalem it is 6 per 1,000. In 75% of the cases it strikes between the ages of 3 and 14. Since full recovery may be effected if the disease is recognized and treated early enough, a campaign of public education has been launched among physicians, teachers, and parents. The only exclusively rheumatic fever ward in the country is at the Bikur Holim Hospital in Jerusalem, with 30 beds. Such a ward is beneficial not only in providing a general program of study and therapy for victims but also in limiting the possibility of these children being infected with other diseases while in the hospital. Schools in Jerusalem may contribute to the incidence of rheumatic fever because they lack central heating.

Hospitalization at the Bikur Holim Hospital ranges from 6 to 13 weeks, with accommodation for convalescents available when needed at the WIZO Baby Home in Jerusalem. About 75 families in Jerusalem, with 100 rheumatic fever victims, have been "adopted" by members of the Rheumatic Fever Society. Food and warm clothing are distributed, jobs are found for an unemployed head of family, and healthier living quarters are arranged. The society also sends volunteer teachers to help children with lessons at home. Three "home to school" telephones have been installed in the homes of children with rheumatic fever, enabling them to participate in class lessons.

Poliomyelitis.—Dr. P. Yekutiel and co-workers reported that in the winter and spring of 1957 a large-scale immunization program against poliomyelitis was understaken in Israel. Salk vaccine, some of which was imported from the United States and some produced locally, was used. The program at first included infants and children 6 months to 3 years old. Of those eligible in this age group, 116,000 received two basic intracutaneous or subcutaneous inoculations of 0.3 to 0.5 ml. of vaccine, 5,500 received one inoculation, and 2,000 none. Later, infants 4 to 6 months old, children 3 to 4 years old, adults who immigrated from the English-speaking countries up to the age of 30, and children in this immigrant group were added to the program. A total of 22,000 of these received two basic inoculations, and several thousand received one inoculation. No vaccine was given between June 1, 1957, and Jan. 1, 1958, when booster inoculations were started. Clinical, epidemiological, and laboratory data were collected on each case of poliomyelitis that occurred in 1957. A total of 57 cases were reported. This number, compared to a five-year annual average of 650 cases in the years 1952 to 1956, constituted a reduction in poliomyelitis incidence of over 90%. Of the 57 cases 7 occurred in January before the effect of immunization could be expected; 22 occurred in nonimmunized infants less than 1 year old who were born in 1957 and, therefore, were not included in the program; 8 occurred in unvaccinated children over 4 years old; and 20 in the "campaign" age group. Of these 20 patients, 11 had received two inoculations of vaccine, 3 had received one inoculation, and 6 none. The immunization seems to have been very effective in reducing the incidence of poliomyelitis in the immunized infants and children. The high effectiveness of the immunization with Salk vaccine may have been due to the fact that almost 95% of the susceptible age groups had received two inoculations of vaccine prior to the poliomyelitis season.

JAPAN

Status of Tuberculosis.—Despite the use of PAS, streptomycin, isoniazid, and highly perfected chest surgery, morbidity from tuberculosis has not shown any sign of diminution, although the death rate has decreased. In other countries sanatoriums are being closed or undergoing a change of function for lack of tuberculosis patients. The causes for this situation will be found in the lack of public funds appropriated for tuberculosis control. Less than 30% of the patients with active cases are being treated in sanatoriums, and only slightly over 20% of all tuberculosis patients receive adequate treatment. Mass surveys are made only once a year, and only about 33% of the population are included in such surveys. As a consequence the number of active cases does not diminish. Each year an estimated 330,000 new cases develop. Tuberculosis hinders the nation's economic growth and is a potent cause of keeping the people impoverished, thus setting up a vicious circle.

Japanese B Encephalitis.—Each May and June there is an epidemic of Japanese B encephalitis. In the 1948 epidemic over 2,000 cases were reported, but in 1957 there were only 100. The disease reaches a peak every 10th year, so health authorities are prepared to vaccinate 500,000 children under 15 this year. The disease is especially dreaded because the case fatality rate is about 33% and the complications in those surviving include imbecility, epilepsy, and other permanent and completely disabling conditions. There is no permanent immunity, but among natives it is rarely seen after age 15.

Artificial Insemination.—The first successful insemination of a human subject was recorded nine years ago, but since then over 1,500 cases have been reported. No insemination of a single woman or a widow has been reported. A case in point recently came up. A young wealthy widow who lost her 7-year-old only child and did not wish to remarry requested a physician to arrange for artificial insemination. This was refused because any child born under such conditions would be judged to be illegitimate.

Isotopes and Tuberculosis.—Radioisotopes are being used as a tracer at Ochuja Sanatorium in Tokyo. Some of the questions to be studied are: 1. Will isotopes directly attack tubercle bacilli? 2. How does the pulmonary edema of tuberculosis occur? 3. How and by what route do streptomycin and other chemotherapeutic agents work? The results may revolutionize the treatment, according to Dr. Adachi.

Marriages Between Relatives.—Although marriages between relatives is prohibited by law, in certain districts where families have dwelt for many generations marriages between distantly related persons are common. It is generally believed that some of the hazards of such marriages include miscarriage, stillbirth, infant death, blindness, deafness, and hemophilia. While in other countries the percentage of such marriages is negligible, in Japan it is about 5%. To correct this situation more stringent laws are being drafted.

Medical Technicians to Be Licensed.—No modern hospital or clinic can operate without the services of the laboratory technician. To further improve their services the government has set a minimum standard of two years of college training as a prerequisite before the technical training can begin. Before being licensed a technician must now pass the state examinations.

NEW ZEALAND

Blood Studies of Maoris.—Lehmann and co-workers (*Nature, London* 181:791, 1958) examined 92 Maoris, of whom 65 were not first-degree relatives. The aim was to obtain a gene pool which represented Maoris without white admixture. Eighty-five belonged to the Tuhoe and seven to the Arawa tribe. All were examined for the Diego blood group, for hemoglobins E and H, and for other abnormal hemoglobin types which can be detected by the sickling test or electrophoresis. In 84 samples a search was made for evidence of thalassemia by examining the cells morphologically, determining the alkali-resistant fraction of the hemoglobin and searching for an increased proportion of hemoglobin A_2. Recent investigations of Mongoloid populations showed in some of them a high incidence of hemoglobin E and of the Diego blood group. Hemoglobin E has been found in Siamese, Burmese, and northeastern Malaysians, and the highest frequencies of the Diego blood group have been found in North and South American Indians, Japanese, and Chinese. Hemoglobin H has been found in some Greeks, in a Jordanian Arab, notably in Chinese and Siamese, and occasionally in Philippinos and Malaysians. Thalassemia or Mediterranean anemia is not restricted to persons of Mediterranean origin, for a high incidence has been reported in Siamese and other Asiatic populations. Previous studies in the Australasian region had so far revealed no abnormal hemoglobins and no examples of the Diego blood group. In the present search no hemoglobin E, H, or any other abnormal hemoglobin, no Diego blood group, and no evidence of thalassemia were found in the Maoris. These findings distinguish the Maoris from the North and South American Indians and from the Siamese, Burmese, and Malaysians. It is of interest that the Diego factor was not found, in view of Heyerdahl's theory of the American origin of the Polynesians.

Identification of Narcotics.—Dr. O. H. Keys, government analyst for Otago and Southland, working in close cooperation with the University of Otago, devised a new technique for identifying narcotics which should be of great practical value. It is based on the bombardment of the material—as little as a fraction of a milligram—by a narrow beam of x-rays. A geiger counter records the angle of diffraction of the rays as a graph. Each material produces a distinctive graph, and it is a simple matter to compare the data with a specially devised reference file. The older chemical method of identification requires careful investigation, sometimes extending to two weeks. It has also the disadvantage that the substance isolated during the analysis is destroyed in the final identification. The new method has the advantages over the classical method that it is instantaneous, unequivocally accurate, and can classify a narcotic without destroying or consuming any of the material.

Lung Cancer.—According to a report from the statistical branch of the Health Department, not one factor but a combination of factors might be responsible for the increase of cancer of the lung and bronchus. The increase in the incidence of and mortality from cancer of the lung has been steady, with 286 pulmonary deaths from this cause in men in 1955 compared with 36 in 1936. The disease has been linked with cigarette smoking, atmospheric pollution, and certain occupational hazards. The incidence was greater in urban and highly industrialized areas than in rural areas, and immigrants from Great Britain showed a higher death rate from lung cancer than persons born in New Zealand of the same stock. The difference was greater in those who came here at a later age than in those who come to this country when young. The hypothesis is that immigrants are affected by their former environment. In contrast to the position in men, cancer of the lung in women is still uncommon in New Zealand. As it would be logical to expect the same relationship between lung cancer and smoking habits in women as in men, this is probably explained by the fact that there are few women over 50 who have been heavy smokers for a long time. Most New Zealand women, in the ages at which lung cancer has the highest incidence among them, are nonsmokers and have always been nonsmokers. Few of even the heavy smokers have been smoking for long.

Infant Mortality in Cook Islands.—Dr. D. D. McCarthy of the University of Otago investigated the high infant death rate in the Cook Islands. In some of the islands the rate is 300 in every 1,000 live births. In New Zealand the rate is about 22 and among Maoris about 74. One startling finding, which may help other research workers and sociologists engaged in enhancing sanitation and welfare in the Southern Islands, was that the islands where the mortality is the highest are those in which the cash incomes are greatest. They have not yet learned what to do with their spare cash. Instead of spending their money on houses and giving more attention to their food, they spent it on clothes, wrist watches, and beer. Their extra spending money came mostly from pearl shells. The first preventive measure taken was to increase prenatal work and infant and child welfare. The Cook Islanders went through a bad economic period several years ago and developed a general sense of frustration. The change in their economic status was too rapid and they have not been able to adapt themselves to it.

SWEDEN

Professional Secrecy.—Since compulsory health insurance came into force on a national scale at the beginning of 1955, the medical profession has been confronted with problems of professional secrecy. The authorities concerned with the administration of health insurance wish to ensure its smooth working and to avoid abuses and to this end have indicated that on sending a patient to hospital his physician should give the reason for doing so. This means that he must more or less commit himself to a diagnosis which thus comes to the notice of the persons employed in the health insurance service. In *Svenska läkartidningen* for March 14, Dr. E. Svennilson pointed out how this proposal may embarrass the physician who sends a patient to hospital because he has become insane, has attempted to commit suicide, or is alcoholic, epileptic, or syphilitic. To protect his patients, the physician is tempted to make use of terminological inexactitudes, to use words comprehensible to scholars only, or to take refuge in the oracular "admission for observation." Svennilson sees no easy solution, but he insists that respect for professional secrecy is essential to the happy cooperation of physician with patient.

Courses in Public Health.—Physicians interested in public health and representing Denmark, Finland, Iceland, Norway, and Sweden meet every August in Gothenburg to discuss public health problems and to pool the experiences of their respective countries in this field. A further objective of these meetings, which enjoy financial support from WHO, is to train in public health physicians capable of holding important appointments in this specialty. Last fall the class of 22 was composed of 6 from Denmark, 4 from Finland, 1 from Iceland, 5 from Norway, and 6 from Sweden. One third had attended two earlier courses, another third one such course, and the rest were newcomers. For the first time the course was attended by two public health nurses. The range of subjects discussed on this occasion was wide and included the care of the aged, alcoholism, drug addiction, and suicides. The last week was spent in Oslo studying Norway's pioneer work on rehabilitation of the unfit, Norway's cancer register, and its welfare program for seamen. It is expected that from these courses a permanent school of public health will evolve.

Junior Physicians Meet.—The Swedish Association of Junior Physicians met in March in Upsala and reviewed the most salient features of the campaign to improve their lot. The chairman, Dr. Olof Johansson, drew attention to the agreement drawn up between the hospital authorities in June, 1957, and the holders of junior hospital appointments with reference to a pensions scheme. This agreement was provisional only. Another problem needing speedy solution concerned finding enough applicants for the many junior hospital appointments recently created. It was countered by an informal agreement between the parties most concerned to ration or rationalize these appointments. Another stumbling block has been the inadequate remuneration of the physicians who lecture to nurses. It was proposed that the fee of 25 Swedish crowns per hour be doubled. What is, perhaps, the most crying need of the medical profession is to be relieved of all the duties which can possibly be discharged by laymen.

Lidocaine for Epilepsy.—Dr. E. Bohm (*Nordisk medicin,* April 10, 1958) treated 48 epileptics with intravenous injections of a 1 or 2% solution of lidocaine. When this treatment was successful it took effect in 30 to 45 seconds—the time taken to complete the circulation of the blood. The injections did not disturb the patient's sense of consciousness, and when the attacks recurred, the treatment was repeated in the form of a continuous intravenous drip with saline or dextrose solution. A single dose of lidocaine was sufficient to arrest 11 of the 12 attacks of grand mal in 7 patients and 19 of the 29 Jacksonian attacks in 22 patients. Ten patients suffering from status epilepticus of the grand mal type were given a continuous intravenous drip on 13 occasions in 7 of which the treatment was successful. Treatment was also successful on 14 of the 20 occasions on which it was given for status epilepticus of the Jacksonian type. The treatment was less effective in attacks of subcortical than in those of cortical origin.

Cycloserine for Tuberculosis.—Dr. I. Ståhle (*Svenska läkartidningen,* April 18, 1958) used cycloserine combined with isoniazid to treat 19 patients with pulmonary tuberculosis. Serving as controls were 23 similar patients who were given a combination of PAS with isoniazid. The two groups were compared with respect to temperature, weight, sedimentation rate, and roentgenographic and bacteriological findings. With the exception of one patient in the control group, there was a rapid fall of the temperature to normal. The sedimentation rate showed marked improvement in both groups, but the roentgenographically demonstrable improvement was definitely better in the cycloserine-treated group than in the controls. A dosage of 0.5 Gm. of cycloserine was well tolerated.

Group Treatment of Alcoholics.—Since February, 1957, a clinic for alcoholics in Linköping has held group discussions for 30 of its patients. G. Wretmark and co-workers (*Svenska läkartidningen,* April 11, 1958) reported that the patients were carefully selected for this treatment, excluding those with mental deterioration, severe personality abnormalities, flaccid or mythomanic characteristics, or serious criminal tendencies. Qualifying for this treatment were depressive, dysphoric, tense, sensitive, aggressive, explosive, and hysteroid alcoholics. At a meeting, the attendance should include at least four and preferably five or six patients with a physician bereft of the paraphernalia of his calling and on his guard not to slip into didactic speech likely to encourage silence on the part of the others. The patient of a domineering turn of mind has to learn not to monopolize the conversation. Meetings attended by too many patients tended to become useless. Meetings were also held for the wives of alcoholics. The follow-up account of how these patients fared showed among other things that only two were not carrying out normal work. There were, however, five who discontinued this treatment at an early stage.

UNITED KINGDOM

Stokes-Adams Syndrome Treated with ACTH.—On the assumption that heart block in Stokes-Adams syndrome might be due to inflammation of the bundle of His, Litchfield and co-workers (*Lancet* 1:935, 1958) treated three patients with this condition with ACTH. An infective or rheumatic origin was suspected in each case. The attacks had previously failed to respond to atropine and adrenergic drugs. In two patients the attacks ceased, with reversion of the electrocardiogram to normal in one. In the third patient the attacks ceased on the day ACTH was given, but they recurred when the dose was reduced. The development of heart failure in this patient necessitated a reduction in the dosage of ACTH. Complete heart block then developed, and the patient died about four months later. Although the prognosis in Stokes-Adams syndrome is unpredictable, it was thought that the improvement in these patients was not due to chance recovery. It is possible that the improvement may not have been due to the suppression of inflammation but to an alteration in the metabolism of the heart muscle. An autopsy on the fatal case showed a cellular reaction with secondary calcification extending across the bundle of His from the diseased aortic valve.

Osteoarthritis.—Ross and co-workers (*Brit. M. J.* 1:1040, 1958) injected 0.1 to 0.3 ml. of 5% benzyl salicylate and 5% camphor in peanut oil into knee joints in 53 patients with osteoarthritis at weekly intervals for six weeks. In addition 18 patients, under light general anesthesia, received an intraosseous injection of 25 to 40 ml. of a solution containing 0.2% salicylic acid and 1% sodium citrate in water in the subcortical areas of the femur and a like amount in the tibia. The patients were followed up for six months after the injections, and an estimate was made of function; of the patient's own assessment of the value of the treatment; and of any change in such physical signs as heat, tenderness, effusion into the joint, and range of movement. Some improvement was observed in 76%. This was graded as excellent in 27%, good in 30%, and fair in 19%. The authors do not believe that the improvement was due to a simple local analgesic effect, as it did not occur until at least 24 hours after the injection and was usually not noticed until after the third or fourth injection.

Routine Medical Checkups.—Although routine medical examinations or health checks are common in the United States they are not in Great Britain, except for those exposed to special industrial or occupational hazards. The value of such checks has recently been questioned in *The Times.* A member of Parliament asked whether public money should be spent by the British Broadcasting Corporation on routine health checks for its senior executives. The Chairman of the B. B. C. replied that the cost involved was a relatively small premium to pay for the maintenance of the health of key personnel. Several well-known physicians then joined in the correspondence, stating that they considered routine examinations of this type virtually useless in the early detection and treatment of disease.

Lancet supported this view. It admitted that sometimes such a periodic health check might be useful but that its advantages are exaggerated. Few disorders can be detected before symptoms appear, with the possible exceptions of diabetes and tuberculosis. Acute conditions may strike down healthy people before symptoms appear, while in many chronic disorders treatment can be given equally well in the later stages of the disease. Such examinations if made routinely would add 280 million dollars a year to the cost of the National Health Service, a sum that might be used more effectively in other ways. Another argument against periodic health checks is that they would create anxiety and neurosis in certain persons. Such examinations are likely to be of value only when a large organization employs a full-time physician to examine personnel at fairly short intervals. He would then be expected, like the general practitioner, to know their social, medical, and occupational backgrounds.

Dental Erosion Caused by Soft Fruit Drinks and Ices.—Mellanby and co-workers (*British Dental J.* 104:305 [May 6] 1958) stated that soft fruit drinks, carbonated beverages, fresh fruit juices, candies known as "acid drops," and frozen synthetic fruit drinks sold as "iced lollies" cause dental erosion. Carbonated beverages are less harmful than the others. Most of the observations were carried out on the teeth of rats and dogs, but some were made on extracted human teeth. Many children suck iced lollies for long periods, and in this way citric or tartaric acid comes in direct contact with the teeth for long periods, causing marked erosion. Sucking fruit-flavored candies, which also contain these acids, is also harmful to he teeth.

Secretion of Hydrocortisone.—Hydrocortisone is one of the major steroids secreted by the adrenal cortex, and measurement of its rate of production is a valuable index of adrenal activity. The need for a simple method of estimating its production by the body led Cope and Black (*Brit. M. J.* 1:1020, 1958) to explore the possibility of using hydrocortisone labeled with radioactive carbon (C^{14}) for this purpose. The principle of the estimation is the well-established one of isotope dilution. If a small amount of C^{14}-labeled hydrocortisone is introduced into the body it may be expected to be metabolized in the same manner as the endogenous hydrocortisone, with which it becomes diluted. It can be estimated in the urine by means of its radioactivity. The activity of a 24-hour collection of urine is measured and compared with the original activity of the ingested hydrocortisone. From the data obtained Cope and Black calculated that the average daily excretion of hydrocortisone is about 13.5 mg. in normal persons, with a range of 5 to 28 mg. In six subjects with severe but nonendocrine disease, the mean daily excretion was 20 mg. The response to routine ACTH therapy was variable, the highest output being 257 and the lowest 21.8 mg. daily, a figure within the normal unstimulated range. In paients with hepatic cirrhosis the excretion rate was slow, and in hyperthyroidism it was high. In hypoadrenalism due to adrenal cortical hypofunction or to hypopituitarism hydrocortisone production was between 0.6 and 1.2 mg. daily with a mean of 0.9 mg. When the activity of the adrenals was inhibited by therapy with prednisone or 9-α-fludrocortisone therapy the excretion fell to 2.3 mg. daily. A hydrocortisone production of only 1 mg. daily was found in a pseudohermaphrodite, confirming the belief that a low output occurs in such patients.

New Gastric Antisecretory Agent.—Douthwaite and Hunt (*Brit. M. J.* 1:1030, 1958) used the new antisecretory agent, Nacton, or (1-methyl-2-pyrrolidyl) methyl benzilate methyl methosulfate, to reduce the gastric secretion of patients with peptic ulcers. This compound has an atropine-like action of long duration and reduces the gastric secretion of hydrochloric acid in response to a test meal without appreciable side-effects. The changes in the gastric secretion of acid were studied in 23 patients with duodenal ulcer and two with gastric ulcer. The stomach was washed out while the patient was fasting, and a 750-ml. test meal containing 50 Gm. of glucose per liter and a dye not absorbed from the stomach was given. After 30 minutes the gastric contents were recovered, the completeness of recovery being checked by washing out the stomach. From the amount and composition of the dye remaining in the gastric contents the amount of the latter that had passed into the duodenum was found, together with the total amounts of acid, chloride, and pepsin secreted. It was then possible to describe the gastric secretion of acid in terms of milliliters of 0.16 N hydrochloric acid, the concentration at which it is produced by the parietal cells. The dose of drug given was that which did not produce side-effects. Initially a dose of 8 to 10 mg. a day was given in divided doses every six hours, and this was increased by 4 mg. daily until side-effects were produced. The dose was then reduced until these just disappeared. Given every six hours, Nacton effected a continuous reduction of gastric secretion to about 50% of the control value in response to a test meal. In patients with marked hypersecretion the inhibition was often greater when expressed as a percentage of the control than in those with lower levels of secretion. There was little change in the rate of gastric emptying and no change in the mean output of gastric nonparietal secretions.

MISCELLANY

SALUTE TO THE MEDICAL PROFESSION

Alex Dreier

Men . . . and medicine. This combination has inspired great thoughts and deeds for 4,000 years, and spells a brighter, healthier future for every human being on earth. Men of purpose, ideals, and highly refined skills . . . general practitioners, radiologists, pathologists, internists, psychiatrists, surgeons, hospital administrators, public health officers, obstetricians, orthopedists, pediatricians. Men like your family doctor—who knows you better than you know yourself.

These are the kinds of men who are the human fabric of the American Medical Association—dedicated to the promotion of "the science and art of medicine and the betterment of public health." And this they have done, to the benefit of all.

To most people A. M. A. is simply a familiar group of letters. "Something to do with doctors" is the pat explanation. Well, it does have something to do with doctors, all right—and with lawyers and bankers and bandits and movie queens and the people next door.

It was born under dramatic circumstances back in 1847 in Philadelphia. There, determined physicians from 22 states met to discuss the inferior quality of medical education in the United States, the disappointingly brisk traffic in harmful patent medicines, and the lack of a recognized code of ethics. These things they discussed, and many more. And from their deliberations came the national association of physicians known as the American Medical Association—a democratic association of more than 70,000 physicians welded into almost 2,000 county and district medical societies. Physicians from all 48 states and Hawaii, Alaska, Puerto Rico, the Isthmus of Panama, and the District of Columbia. A big, busy organization with its own national legislative body, which includes delegates from the Army, Navy, and Air Force, the Veterans Administration, and the Public Health Service.

The A. M. A. works through its councils, bureaus, departments, and committees. It is concerned with everything you can think of, and dozens of things you may not: education, chemistry, nutrition, rehabilitation, industrial and rural health and research, medical motion pictures, publications, and pesticides.

The A. M. A. performs so many services, both seemingly simple and deceivingly complex, that it would be futile to attempt to enumerate them here. But what does it do for the public? What, as the man says, is in it for me?

First of all, it promotes health. It produces films on health, and cooperates in both local and network radio and television programs concerned with health and better living.

Through newspapers, magazines, and other media the Association's public relations department produces authentic health news and issues a widely used weekly news release, as well as huge quantities of special releases concerning the association's annual and clinical sessions. A staff cooperates with writers of all media in collecting medical literature, checking references, and arranging interviews with medical authorities.

It also publishes books, pamphlets, booklets, special reports, and the widely read magazine *Today's Health.* And it answers questions—endless questions on an endless variety of health problems. As many as 15,000 letters annually pour into its Health Education Bureau, out of the almost 24,000 letters that inundate staff employees at A. M. A. headquarters in Chicago each week.

It even maintains a Bureau of Investigation, a sort of medical F. B. I., without actual police powers but with a highly effective organization to probe the thousands of complaints involving the unscientific side of medicine. Law enforcement agencies have frequently used this bureau's information and files to crack down on quacks. Other specialized councils or committees examine food and cosmetics and drugs and devices of all kinds, insuring their purity, effectiveness, and safety.

And the Association also maintains inspection and consultation services for medical schools and hospitals, resulting in a tremendous upgrading of standards, better-trained physicians, and higher-quality medical care for the American people.

Out of the wealth of bills introduced on medical subjects, the A. M. A. selects and supports those with primary medical implications, the promise of real benefit to the public. It also throws its considerable support and prestige behind measures it considers essential to the well-being of the nation as a whole—backing food and drug laws, hospital construction acts, and bills supporting the United States Public Health Service, for example.

Yesterday's physician carried a small black bag containing a half-dozen instruments to take care of your ills. Today's physician keeps a well-equipped office embellished with modern, complex mechanical and electronic aids. He also uses the great facilities of modern hospitals and laboratories. And most of all, despite the busiest era in the history of modern medicine, he continues to educate himself. Don't ask us where he finds the time or how—we cannot imagine. We know only that he does, somehow, find the minutes and hours to digest a wide variety of pamphlets, books, reports, articles, and

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From "America on the Go" broadcast over NBC-Monitor, Sunday, June 22, 1958, 6:05 p. m. EST.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Treatment of Hypertensive Heart Failure and of Hypertensive Cardiac Overload by Blood Pressure Reduction. F. H. Smirk, M. Hamilton, A. E. Doyle and E. G. McQueen. Am. J. Cardiol. 1:143-153 (Feb.) 1958 [New York].

The introduction of ganglion blocking agents provided an effective method of reducing blood pressure and of maintaining the blood pressure of patients with hypertension at, or near, normal levels. It has been demonstrated that reduction of blood pressure alone, without the use of digitalis, mercurial diuretics, or salt restriction, is sufficient to relieve the symptoms of hypertensive heart failure. The authors report their experience in the treatment of 310 patients with hypertensive heart failure with ganglion blocking agents—hexamethonium bromide initially, and latterly pentolinium (Ansolysen), chlorisondamine (Ecolid), and mecamylamine (Inversine). It is of fundamental importance that the systolic blood pressure, in the trough of the blood pressure fall, should be decreased to between 120 and 135 mm. Hg. At this level of systolic blood pressure the diastolic blood pressure will also be satisfactory. Many of the less satisfactory results obtained by the authors were in patients in whom side-effects made it impracticable to reduce the cardiac overload to this extent. The patients were followed for periods of between 2 and 7½ years.

There were 4 groups of patients. In the first group, of 41 patients with left ventricular failure only, 35 were controlled without recourse to digitalis, mercurial diuretics, or salt restriction. Thirteen of these patients have died. In the second group, of 44 patients with combined heart failure, 38 of whom also had attacks of nocturnal dyspnea, 20 were relieved without ancillary measures. Of this group, 22 have died so far. Thus, 35 of the 85 patients with heart failure have died. The average duration of treatment of those who have survived is 50 months, and the duration of treatment of those who died was 23 months. Forty of the 50 surviving heart-failure patients are able to work.

The third group comprised 127 patients who had dyspnea on exertion but no failure. Four of these patients later died of heart failure. In addition, there were 26 other deaths, including 12 from cerebral vascular accidents, 7 from cardiac infarction, 5 from uremia, and 2 from various other causes. The fourth group of 98 patients had neither failure nor dyspnea but had moderate to severe hypertension. In this group 5 patients died of congestive failure. In addition, there were 26 other deaths, including 15 from cerebral vascular accidents, 3 from cardiac infarction, 5 from uremia, and 3 from other causes. The authors conclude that in hypertensive patients heart failure results more from cardiac overload, rather than from irreversible muscle damage, and that it can be prevented or controlled solely by measures to reduce the blood pressure.

Chronic Myocarditis. S. Van Creveld and H. A. P. Hartog. Nederl. tijdschr. geneesk. 102:211-215 (Feb. 1) 1958 (In Dutch) [Amsterdam].

The authors present the histories of 3 patients, a 25-year-old man, a 9-year-old boy, and a 40-year-old woman, who died of cardiac decompensation resulting from chronic myocarditis. In the course of years interstitial myocarditis developed, with extensive fibrosis of the heart muscle. One patient presented a syndrome suggestive of constrictive pericarditis. The authors cite several literature reports on cardiac dilatation and decompensation caused by chronic myocarditis. In some of these reports, as in the patients here presented, there were no signs of endocarditis or pericarditis. The histological picture did not resemble that of rheumatic myocarditis. Resistance of the cardiac decompensation to all therapeutic measures has also been described previously, and it has been suggested that a virus infection might be the cause.

Antibacterial Therapy of Pulmonary Tuberculosis. F. V. Shebanov, V. S. Gavrilenko, T. F. Smurova and V. N. Adamovich. Sovet. med. 21:58-63 (No. 12) 1957 (In Russian) [Moscow].

Shebanov and his associates state that treatment of active pulmonary tuberculosis must be carried out in a hospital so as to make possible administration of antibacterial drugs, collapse therapy, or surgical procedures. Hospital treatment for 3 to 4

The place of publication of the periodicals appears in brackets preceding each abstract

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months is to be followed by treatment in a sanatorium for 7 to 10 months. After the patient has been discharged from the sanatorium, the administration of antibacterial drugs is continued for 3 to 6 months. Reversal of primary progressive tuberculosis requires about 2½ years. Treatment of primary tuberculosis in its infiltrating phase is commenced with a combination of streptomycin and PAS. To avoid the development of streptomycin resistance, this drug after 2 months is replaced by phtivazid, which after being given for the next 2 to 3 months is followed by 1 to 2 months' courses of streptomycin in combination with either phtivazid or PAS for the next 6 months. The entire course of treatment of an adult patient requires 120 Gm. of streptomycin, 240 Gm. of phtivazid, and 3,600 Gm. of PAS.

Tuberculous lymph nodes are treated for 1½ to 2 years with the administration of the 3 antibacterial drugs, streptomycin, PAS, and phtivazid, by interrupted courses. Acute miliary tuberculosis requires the combined administration of the 3 drugs for the first 3 months. The treatment is continued for 10 to 12 months. Acute limited destruction of pulmonary tissue requires 1 to 2 months of treatment with streptomycin and PAS to be followed by artificial pneumothorax if the process is not terminated. This is to be followed by treatment for 3 to 4 months with phtivazid and PAS. In caseous pneumonia the authors resort to combined treatment with streptomycin, phtivazid, and PAS administered for 3 to 4 months. Further treatment is continued for 4 to 5 months with phtivazid combined with PAS. This is followed by interrupted courses with streptomycin and PAS. This therapy diminishes the toxicity and aids in the transition of the process into the chronic, fibrous, cavernous tuberculosis. The duration of treatment of caseous pneumonia is from 1 to 2 years. A number of patients with fibrous, cavernous tuberculosis require radical surgical treatment. Surgical interventions are preceded by treatment with streptomycin and PAS.

The effect of the antibacterial drugs upon the chronic types of pulmonary tuberculosis, especially those of the cavernous type, is sometimes ineffective. For such cases the authors advise tuberculin therapy and repeated transfusions of small amounts of blood. Tuberculin is given subcutaneously, beginning with a small dose which is increased by 0.1 to 0.2 cc. every 5 to 6 days until 12 to 15 injections have been given in the course of 2 to 3 months. Tuberculin therapy is particularly indicated in cases of long-continued infiltrative and focal tuberculosis with continued intoxication, hilar infiltrates, and cirrhotic process with some destruction and involvement of peripheral lymph nodes. Transfusions of 30 to 50 cc. of blood once a week are performed 8 to 12 times. Blood transfusion is particularly indicated in exudative pleurisy and in serous and purulent pleuritis. The introduction of antibacterial therapy in the treatment of pulmonary tuberculosis has not completely solved the question of treatment of cavities. Complete closure of cavities is observed rather rarely with this type of therapy. Recurrences develop 1 and 2 years after treatment. The employment of pneumothorax in combination with antibacterial therapy increases the percentage of positive results.

The Intradermal Test in Tularaemia with Particular Reference to the Reaction Elicited in Regions of Different Incidence of the Disease. O. Ljung. Acta med. scandinav. 160:135-147 (No. 2) 1958 (In English) [Stockholm].

The investigations described were undertaken to investigate the test with Pasteurella tularensis antigen and to obtain a definition for the positive reaction that would establish whether tularemia infection has definitely occurred. To judge from the literature and the author's own experience, persons with manifest tularemia always seem to present a clearly positive reaction. The study also included observations of the intradermal test in other classes of subjects. The intradermal test with antigen consisting of chemically inactivated Pasteurella tularensis was performed on 3,211 persons. A dose of 0.1 ml. was administered intracutaneously on the volar aspect of the forearm. Of the persons tested, 40 had had manifest tularemia 2 to 21 years previously (mean, 7½ years). The other persons had never been known to have the disease. They were from areas with different incidences of tularemia. Reactions to the intradermal test ranged from completely negative to strongly positive, with areas of edema of mean diameter up to 100 mm. The reaction was read at 72 hours. A positive reaction was defined as one in which there was an area of edema with a mean diameter of 7 mm. or, if vesicles or pustules were present, at least 5 mm. A lower criterion for a positive reaction would result in nonspecific reactions falling in this class.

Of the 40 patients who had had tularemia 2 to 21 years previously, 36 (90%) gave positive responses. Of 131 tests on hospital patients from areas where tularemia was unknown, none was positive. It is evident from this that the intradermal test is a fairly reliable means of demonstrating past infection and that nonspecific positive reactions are rare. In 472 hospital patients from areas with a low incidence of tularemia, 7 positive reactions were found (1.5%). Of 2,047 persons from areas where there was a high incidence of the disease, 227 (11.1%) gave a positive reaction. There was no difference in the type of the positive reaction in those who had had tularemia and those who had not, although, as a rule, the former presented a stronger reaction. However, of the 17 persons with the largest areas of edema, 10 had not, as far as they were aware, had tularemia. These positive reactions must be ascribed to atypical, abortive, or symptomless tularemia. According to the literature, nonspecific reactions have not been observed. Through some error in the preparation of the test solution, however, several patients in the 2 last series had strong nonspecific reactions. When 432 (76.2%) of 567 subjects gave positive reactions, further study showed that these reactions were due to an irritant in the dilution medium and not to the inactivated Pasteurella tularensis.

Intradermal and Agglutination Tests in Tularaemia, with Particular Regard to the Demonstration of Past Infection. O. Ljung. Acta med. scandinav. 160:149-154 (No. 2) 1958 (In English) [Stockholm].

The investigations in the preceding paper had shown that 90% of persons who had had tularemia 2 to 21 years previously gave a positive response for the intradermal test. When the agglutination test was performed on 36 of these patients, 6 exhibited negative agglutination reactions. Of 151 subjects with no history of tularemia but with positive intradermal reactions to killed Pasteurella tularensis antigen, only 47 exhibited positive agglutination tests. As previous studies by the author have shown, it appears likely that these 151 persons had previously had an atypical, abortive, or asymptomatic attack of tularemia. The high proportion of negative agglutination reactions in these persons was unexpected. Simultaneous intradermal and agglutination tests were performed on 104 consecutive hospital patients who, although they had no history of tularemia, were from an area where there was such infection. Twelve persons gave a positive intradermal test. In only 2 cases was a positive agglutination reaction (and a positive intradermal reaction) elicited. These reactions do not show parallelism, and occasionally one may find positive agglutination reactions and negative intradermal reactions, but, on the whole, the intradermal test appears to be the better for demonstrating past tularemia. The intradermal test with killed Pasteurella tularensis seldom appears to give rise to positive agglutination reactions to this antigen. Ninety-two subjects still gave a negative agglutination reaction 4 to 9 weeks after an intradermal test.

Kidney Biopsy in Acute Glomerulonephritis. C. Brun, H. Gormsen, T. Hilden and others. Acta med. scandinav. 160:155-163 (No. 2) 1958 (In English) [Stockholm].

Aspiration biopsies were performed on 13 patients with glomerulonephritis. Judging from the case histories and the clinical findings, all the patients were considered to have acute glomerulonephritis. Seven cases were severe, the 24-hour endogenous creatinine clearance ranging between 0 and 3 ml. per minute. At biopsy all the patients but 1 showed severe changes, all the glomeruli being uniformly and severely damaged. These 6 patients died during the acute stage. One patient had a few glomeruli with some intact capillary loops; this patient was treated with dialysis but died 9 months later. Six cases were mild, the 24-hour endogenous creatinine clearance varying between 46 and 116 ml. per minute. Correspondingly, the changes seen at biopsy were moderate. All 6 patients recovered. On the basis of the criteria generally accepted in evaluating the pathological changes in glomerulonephritis, the histological pictures observed in the biopsies were considered subchronic or chronic changes in many of the patients. This discrepancy between clinical and histological pictures might be due to the fact that some of the patients had acute exacerbations in a chronic disease. This possibility could, however, be excluded in at least 1 of the patients. Another explanation is that the histological changes in the glomeruli were considered of older standing than they actually were. As the technique of kidney biopsy provides the possibility of seeing the earliest stages of the acute disease, the concept of the histological picture at these stages might have to be revised.

Prevalence, Nature and Identification of Leukocyte Antibodies. J. L. Tullis. New England J. Med. 258:569-578 (March 20) 1958 [Boston].

Increasing awareness of the role of autoimmune mechanisms in the production of certain types of idiopathic hemolytic anemia and thrombopenic purpura has stimulated work on the possible relation of idiopathic leukopenia to autoantibody formation. As a first step in large-scale identification of naturally occurring leukocyte antibodies, it was deemed necessary to develop a reliable test. Such a test is described. The effects of mixtures of normal leukocytes and heterologous leukocyte serums (rabbit antihuman white blood cell serums) were observed. The constant findings in such mixtures were decreased motility of the neutrophils, agglutination, and, in the more potent antiserums, hyper-Brownian movement and lysis. If the ameboid motility of the cells was quantitated, it was possible to calculate the decrease in absolute numbers of viable (motile) cells during the test period. For the purposes of this study, an arbitrary standard, the lysis index, was defined as the product of percentage decrease in white blood cell count times the percentage decrease in motile forms. The resulting empiric values gave a marked difference between normal and pathological serum. A lysis index (60-minutes percentage decrease in white blood cell count times 60-minute percentage decrease in ameboid forms) between 0 and 25 was established as representing a normal serum. The index for normal serum averaged 4. Abnormal serums showed an average decreased white blood cell count of 23% at 30 minutes and 35% at 60 minutes plus a decreased ameboid motility of 18%

of the aged may lead to a longer convalescence than usual. Unexpected failures, with complications and possibly death, may, however, occur even in apparently favorable cases.

Exfoliative Cytology of Gastric Carcinoma. R. O. K. Schade. Brit. M. J. 1:743-744 (March 29) 1958 [London].

In an attempt to achieve earlier diagnosis of carcinoma of the stomach, while the tumor is still confined to the mucosa, 2,500 gastric cytological examinations were performed. Lavage with 100-200 cc. of sodium chloride or Ringer's solution was used for obtaining cell material. Twenty-five cases were discovered by this method, in which other investigations by x-ray and gastroscopy were negative. The best material for cytology was obtained from those patients in whom the malignant lesion was subsequently found to be small, often confined to the mucosa. Paradoxically, the material most difficult to interpret comes from those patients in whom the tumors are large and widely ulcerated. The lavage fluid of these cases contains much debris and many organisms and inflammatory cells which make cytodiagnosis difficult or impossible. Patients with an achlorhydria which is always associated with structural mucosal changes, such as a diffuse chronic atrophic gastritis, should be investigated until it has been proved that there is no evidence of carcinoma. Cytological examination, to which few patients object, is an easy method for screening and following up. The gastric cellular material reflects better than any other method the pathological processes of the entire gastric mucosa and can provide satisfactory diagnostic results which compare favorably with radiologic and gastroscopic findings.

Serum Glutamic Oxaloacetic Transaminase, Lactic Dehydrogenase, and Glutamic Pyruvic Transaminase Activity in Evaluation of Heart Muscle Damage. J. S. La Due. Am. J. Cardiol. 1:308-314 (March) 1958 [New York].

Myocardial infarction was produced in dogs by the injection of plastic spheres into the coronary sinus. In every experiment the serum glutamic oxaloacetic transaminase (SGO-T) activity rose promptly with peak levels appearing 9 to 23 hours after infarction. Fifteen infarcts, produced in dogs by tightening a ligature 10 days after it had been placed about a coronary artery, were all associated with an increase in the SGO-T activity. Both the height and the duration of increased enzyme activity appeared to be proportional to the size of the infarct. In similar experiments on 7 dogs in which infarcts were produced, the SGO-T activity increased 3 to 10 times, the serum glutamic pyruvic transaminase (SGP-T) activity increased 3 to 5 times, and the serum lactic dehydrogenase (SLD) activity increased 2 to 3 times over the normal.

Serums obtained within 12 to 48 hours after the onset of unequivocal acute transmural myocardial infarction and daily thereafter in 300 patients were anaylzed for SGO-T activity. In all but 3 patients when the serum was obtained at the time of acute infarction, the SGO-T activity rose 2 to 20 times over the normal within the first 48 hours. The height and the duration of the increased SGO-T activity appeared to be roughly proportional to the size of the infarct as estimated electrocardiographically. Secondary elevations of SGO-T activity were seen after recurrent chest pain caused by the extension of the infarction or the occurrence of a new infarction in the same patient. In 10 patients with acute transmural myocardial infarction, in whom the activity of all 3 enzymes in the serum was studied, the SGO-T activity increased 2 to 20 times over the normal, the SLD 2 to 10 times over the normal, and the SGP-T 1 to 3 times over the normal. No correlation was found between the SGO-T activity and the white blood cell count, the erythrocyte sedimentation rate, the presence or absence of shock, the absolute levels of the blood pressure, the presence of heart failure, the location of the infarction, or the use of anticoagulant drugs.

The SGO-T activity was studied in 50 patients with coronary insufficiency whose electrocardiograms showed evidence of ischemia, as manifested by moderate to marked T-wave inversion sometimes associated with ST-segment changes but without Q-wave abnormalities. The SGO-T activity remained within normal limits in 34 of these patients despite the persistence of prolonged substernal pain. The SGO-T activity rose in 16 of the 50 patients, suggesting acute heart muscle cell damage. In 8 patients pain had been present for 3 to 6 days before the SGO-T activity increased. Angina pectoris or coronary insufficiency is not associated with a rise in SGO-T, SLD, and SGP-T activity unless it is presumably accompanied by heart muscle cell damage. The SGO-T activity in patients with acute rheumatic fever without carditis was not elevated. In some, but not all, patients with extensive rheumatic carditis, the SGO-T activity was increased. The SGO-T activity was followed during the course of pulmonary infarction in 7 patients and remained normal in all but 1 patient whose peak enzyme activity was 80 units.

The SGO-T test is of diagnostic value as a specific index of the presence and size of acute heart muscle cell necrosis. SGO-T activity has proved particularly useful in deciding whether acute heart muscle cell damage has occurred when chest pain, like that seen with myocardial infarction, develops in patients with equivocal electrocardiographic changes. In such patients, if the SGO-T activity is carefully followed throughout the duration of pain and for 4 to 12 days thereafter, many patients may be saved weeks of invalidism or anticoagulant therapy may be instituted to prevent impending infarction. Acute myocardial damage must be presumed to be present in patients with chest pain and equivocal electrocardiographic changes, who have increased SGO-T activity in the absence of known active liver disease. The SGO-T activity will usually help distinguish acute pericarditis and pulmonary infarction from acute myocardial infarction. Further study is needed to evaluate the significance of alterations of SGO-T activity in patients with acute rheumatic carditis.

Porphyria: Report of Nine Cases Diagnosed in the Greater Hartford Area, Including a Family with three affected Members. M. J. Seide. New England J. Med. 258:630-635 (March 27) 1958 [Boston].

Two patients died of acute intermittent porphyria within a 6-month period in hospitals of the Greater Hartford area. To determine the frequency with which this diagnosis has been made, all cases coded as porphyria were pulled from the record rooms of several hospitals located in the Greater Hartford area. A total of 9 cases (4 of them previously reported) were found and are presented in this paper, together with a brief review of the pertinent literature.

Two main groups of porphyria are recognized. One, porphyria erythropoietica, is inherited as a Mendelian recessive; it is characterized early in life by photosensitivity, reddish teeth, red urine, increased hemolysis, increased erythropoiesis, excessive and abnormal porphyrin formation in bone, and splenomegaly. The urine contains increased amounts of uroporphyrins, small amounts of coproporphyrins, but no porphobilinogen. Porphyria hepatica, the other main group, is so named because abnormal porphyrins are believed to be formed in the liver. Acute intermittent porphyria is the most common subgroup. Individual attacks may be long or short. The patient has abdominal pain, peripheral neuropathy, and mental disturbances, with any or all of the following signs and symptoms: hypertension, dilated pupils, attenuation of retinal arterioles, tachycardia, restlessness, cold and clammy extremities, steady or colicky abdominal pain, intestinal spasm, decreased peristalsis, obstipation, urinary retention, or cremasteric spasm. Another subgroup, porphyria cutanea tarda, is often confused with porphyria erythropoietica. However, this form usually begins in the 4th or the 5th decade of life. Photosensitivity, skin pigmentation, and hepatic dysfunction are present; the urine is red, zinc porphyrin is present, and liver porphyrin is increased. Porphyria cutanea tarda is a chronic disease. Death is due to liver failure. There are usually no abdominal or neurological manifestations.

The term "mixed porphyria" describes cases with symptoms of both porphyria cutanea tarda and acute intermittent porphyria, which may or may not appear simultaneously. Latent porphyria is most commonly found in relatives of patients with acute intermittent porphyria. The heredity of acute intermittent porphyria is as a Mendelian dominant, not sex-linked. Several affected families have been reported, and cases 7, 8, and 9 of this report concern a sister, a brother, and their mother. The mother of the 2 siblings had died in 1936. The weight of evidence that she had porphyria is overwhelming, but if her 2 children had not died and if no one had searched the microfilmed files for her record, this case would have remained recorded as "chronic salpingitis and encephalomyelitis." Porphyria is seldom diagnosed unless it is considered. Signs and symptoms are protean. The diagnosis depends on urine tests. Every patient admitted with abdominal pain, bizarre nervous system disease, or psychiatric difficulties should be examined for acute intermittent porphyria, and a specimen of his urine should be allowed to stand exposed. Factors considered to be "precipitating factors" may be early symptoms. Treatment is symptomatic and supportive. Many cases of porphyria, especially mild ones, are overlooked. Even in the 4 severe cases reported in this paper, all terminating fatally, the diagnosis was missed on several previous admissions.

Considerations on Therapy and Prognosis of Recent Myocardial Infarction. B. Jasiński. Schweiz. med. Wchnschr. 88:264-269 (March 15) 1958 (In German) [Basel, Switzerland].

The author reports on 58 women and 86 men, between the ages of 30 and 80 years, with recent myocardial infarction, who were treated at the medical clinic of the Canton Hospital in Winterthur, Switzerland, between 1950 and 1957. Of the 144 patients, 73 died, a mortality rate of 50.5%; the myocardial infarction itself was the cause of death in 35, pulmonary infarction in 15, and cardiac insufficiency in 23. Eighteen of the patients had diabetes mellitus, 21 had hypertension, 8 had chronic disease of the kidneys, 2 had cirrhosis of the liver, and 31 had previously suffered damage to, or insufficiency of, the myocardium as a result of coronary arteriosclerosis with or without hypertension. Of the 144 patients, 30 were in bad condition on admission, with shock, pulmonary edema, and gallop rhythm, and 24 of these died within the first 3 days after admission; if one excludes these patients with a particularly unfavorable prognosis, 114 remain, and 43 of these died, representing a mortality rate of 37.7%. Of the 114 patients, 66 were given anticoagulant therapy, and 48 did not receive anticoagulants. Thirty-two (66.6%) of the 48 patients died, and 12 (18.2%) of the 66 patients died. Dangerous complications, such as pulmonary infarctions and peripheral arterial emboli, occurred already within the first and the second week after the myocardial infarction. Of the patients treated with an anticoagulant, only 4 had these complications, while 27 of those who did not receive anticoagulant therapy had such complications. With the help of an early-instituted anticoagulant therapy, it is possible to bridge this dangerous period.

The author believes that all patients with myocardial infarctions—except those with the well-known contraindications, including peptic ulcer, cirrhosis of the liver, and hemorrhagic diathesis—should be treated with anticoagulants, irrespective of whether they are to be considered as good or bad risks. Of the 58 women reported on, 57 were over 50 years of age, while of the 86 men, 12 were between the ages of 30 and 50 years. These data show that myocardial infarction occurs at an earlier age in men than in women. The risk of myocardial infarction in women coincides with the approaching menopause, and that in an abrupt way and without those fluent transitions by which the time of the occurrence of myocardial infarction is characterized in men. The coincidence with the menopause partly seems to be the result of a reduced estrogen production.

A group of 40 patients, 28 men and 12 women, with myocardial infarction were treated with a proprietary preparation of protein-free animal heart muscle extract (Recosen). Thirty-one patients, 20 men and 11 women, who did not receive Recosen served as controls. Although the course of the electrocardiograms did not differ in these 2 groups, the clinical course of the patients treated with Recosen was less eventful, particularly because of the damping effect of the drug on the extrasystoles. Only 3 of the 40 patients required glyceryl trinitrate for more than 10 days, as compared with 8 of the 31 patients. In addition to the well-known coronary dilator effect of Recosen, this drug exerts a direct influence on the metabolism of the myocardium, as was shown with the aid of the isotope technique (radioactive vitamin B_{12}). Recosen is a valuable adjuvant in the treatment and after-treatment of myocardial infarction.

Diagnosis of Atherosclerosis: I. Correlation Between Clinical Diagnosis, Serum Cholesterol and Low-Density Lipoproteins, and Resting and Exercise Electrocardiograms. H. Engelberg. Am. J. Cardiol. 1:315-322 (March) 1958 [New York].

Serum cholesterol determinations and ultracentrifugal determinations of low-density lipoprotein levels shown as atherogenic index values were performed on, and electrocardiograms and ballistocardiograms at rest and after a double 2-step exercise test according to Master's criteria were obtained from, 560 adult patients, between the ages of 21 and over 61 years, in private practice. There were 149 patients with a history of old myocardial infarction and 349 patients with no clinical evidence of severe coronary, peripheral, or cerebral atherosclerotic disease. Of the 149 patients, 103 were men and 46 were women, and of the 349 patients, 260 were men and 89 were women. In the group without evidence of atherosclerotic disease up to the age of 50 years, the serum cholesterol level did not differ significantly between the sexes, whereas the atherogenic index was significantly lower in women, thus paralleling the known lower incidence of atherosclerosis in women before the menopause. Patients with a history of myocardial infarction had significantly elevated lipid levels at all ages. Although the serum cholesterol and atherogenic index values were usually parallel, when the lipid parameters were divergent, the lipoprotein determination was more accurate than the serum cholesterol determination as related to the clinical diagnosis. The serum cholesterol and lipoprotein values were high in 27 patients in whom peripheral atherosclerotic disease was the presenting illness. In 100 patients with hypertension, the average lipid values were significantly elevated in those patients who had experienced a coronary or a cerebral incident. The lipid measurements correlated directly and significantly with the severity of the electrocardiographic findings at rest and after exercise. The combined application of the various tests will frequently aid in the earlier diagnosis of atherosclerotic disease and in the selective application of prophylactic measures.

Autogenous Vaccine in Prophylaxis of the Common Cold. J. M. Ritchie. Lancet 1:615-618 (March 22) 1958 [London].

The author, director of a public health laboratory in Birkenhead, England, had given over a period of 20 years autogenous vaccines against colds to 60 or 70 persons who requested such treatment. Although no special investigations were possible, it gradually became apparent that almost the only failures occurred in some cases of long standing, where it was practically certain that degenerative changes had taken place in the mucous membrane. In a few cases the improvement might be explained on psychological grounds, but the series was becoming too long for this explanation to be sufficient. As a result of these and other findings, the opinion was formed that the common cold might be due to 2 factors—the virus, whose function is essentially depressive, and an invasion by the patient's own normal but heterogenous secondary organisms, which are usually present in a state of equilibrium, overstepping the mark only as a result of the patient's depressed resistance caused by the virus. If this explanation is correct, these volunteers, experiencing the prodromal stage for a day or 2, kept on catching cold as far as the virus was concerned, but they were immunized against the effects of their own organisms.

In the winter of 1955-1956, studies were made on 184 volunteers; 109 were given weekly injections of autogenous vaccines from their own nasopharyngeal flora and 75 were given carbol saline only. The number of volunteers continuing the vaccine injections was 109 for each of the first 2 months, and 51 for each of the next 3—i. e., a total of 371 volunteer-months for the whole period. The corresponding figure for the controls was a constant 75 for each month—i. e., a total of 375 volunteer-months. In the vaccinated there were 13 full colds in the 371 volunteer-months as against 77 in 375 volunteer-months in the controls. The cold rate per month for the controls was 5 times that of those who were vaccinated throughout the course. The rate of absence from work through "colds" and "upper respiratory infections" was also greater in the controls.

Antibiotics in Small Doses for the Common Cold. J. M. Ritchie. Lancet 1:618-621 (March 22) 1958 [London].

Although the author had encouraging experiences with autogenous vaccines in the combat of the common cold, he feels that mass vaccine treatment is impracticable. He decided to try a controlled short-term antibiotic therapy after ascertaining the sensitivity of the patient's pharyngeal flora before the winter began. If vaccines had given a degree of active immunity, then suitable antibiotic tablets, given at the beginning of the prodromal stage, might well give sufficient passive protection by depressing the pharyngeal flora temporarily to correspond to the depression of the patient's resistance. To avoid risk of producing insensitive strains of bacteria or of disturbing permanently the balance normally maintained between patient and pharyngeal flora, the author decided to try the effect of brief local application only. After preliminary trials had shown that the sucking of lozenges did reduce the number of pharyngeal flora but that this effect was temporary, invitations to cooperate were sent to some of the larger works in the neighborhood.

Studies were made on 919 volunteers from October, 1956, to April, 1957. These were divided into 2 groups; 581 volunteers received short-term antibiotic treatment when they felt a cold beginning, and 338 received an inert tablet. In the treated group, the number of prodromal stages reported was 287 (49%), of which 22 (7%) went on to full colds. In the control group, the prodromal stages numbered 182 (54%), of which 87 (48%) went on to full colds—i. e., 4 colds per 100 volunteers in the treated and 26 per 100 in the control group. The figures for adults were 2.6 colds per 100 volunteers and 23.1 colds per 100 controls respectively. The small dosage of antibiotics used had no permanent effect on the sensitivity of the pharyngeal bacteria or on the proportions of the various species. Some volunteers had irritation of the throat and tongue. It is suggested that, after sensitivity tests have been done, a controlled stort-term antibiotic therapy can, without risk, drastically cut down the effects of the common cold. This method can easily be applied in industry by any well-staffed medical center cooperating with a laboratory.

Antihistaminic "Protective" Sera, Applied to the Treatment of Asthma and Other Syndromes Termed Allergic. R. Benda. Presse méd. 66:455-457 (March 15) 1958 (In French) [Paris].

Certain human serums possess the property of protecting the guinea pig against the toxic action of histamine. This fact, which was established by the author and his co-worker Urquia in investigations that began in 1947, applies in principle only to serums that are spontaneously protective as the result of a natural and constant antihistaminic resistance. On the other hand, a greater or less lack of protective potency in the serum, as well as possible variations, characterizes a particular terrain designated as asthmogenic or, more commonly, allergic in patients with various allergic conditions. These essentially experimental data have given rise to a new therapeutic concept, which is to reproduce in patients with asthma or other allergic diseases the state of antihistaminic protection obtained in the guinea pig with a single injection of protective serum. Spontaneously protective serums are hard to get, since they are found only in 10% of even apparently healthy donors. Inactive serums, however, may in various circumstances acquire (or recover) all or part of the antihistaminic properties in which they are deficient. The acquired antihistaminic properties of serum are particularly noticeable when they develop under the influence of favorable medical treatment, regardless of its kind. The protective power of the serum was calculated in 100 patients with asthma who were subjected to various treatments (injection of protective serum, of deltacortisone, and of protective serum in association with deltacortisone). In 59 of 76 patients who showed an undeniable clinical improvement, there was an evident increase in the coefficient of protection (p), so that p exceeded 70 in 21 patients and even reached 100 in 2. Only serums with a p value equal to or higher than 70 should be regarded as protective; a p value between 40 and 70 provides relative protection, and a p value between 10 and 40 gives only a hint of protection.

Good results of variable duration were obtained in about 70% of 2,393 patients with asthma, usually by a single subcutaneous injection of 2 cc. of protective serum (children under 5 years of age were given only 1 cc.). The beneficial effects lasted in

Arteriography was generally delayed until the patient was conscious. An average of 12 days elapsed between onset of hemorrhage and arteriography. Ligation of the carotid vessels was done shortly after arteriography, frequently the same day. In 8 patients arteriography was performed via the patent carotid artery 1 week to 1½ years after ligation. In no instance was the involved carotid vessel or the aneurysm visualized. Ligation of a carotid vessel was generally accomplished by lightly ligating the vessel so as to approximate the intima without crushing it and then firmly and tightly ligating the vessel proximal to this first ligature. It was hoped to reduce the possibilities of a propagating thrombus developing. The ligation was done with the patient under local anesthesia, and the patient was observed for development of focal neurological signs over a period of 20 to 30 minutes while the artery was occluded and before the wound was closed. A second principle of ligation was to prevent collateral circulation through the external carotid vessel, and therefore the internal carotid artery itself was primarily or secondarily closed off or else the external carotid artery was ligated together with the common carotid artery.

Eighteen of the 19 patients have survived from 6 months to 7½ years after operation (an average of 3⅕ years) without evidence of recurrent hemorrhage. There was 1 immediate postoperative death, and 1 patient is permanently incapacitated with a hemiplegia. Seventeen patients are economically useful. There were 6 postoperative hemiplagias, of which 3 cleared completely and 2 have improved sufficiently for the patients to work. From these results, and a review of the literature, it appears at this time that there is no necessity of attacking this type of aneurysm intracranially. Ligation of the internal carotid artery at an interval after ligation of the common carotid artery appears to be safest as regards prevention of morbidity. The age of the patient at the time of ligation does not seem to influence morbidity.

Results of Surgical Treatment of Pulmonary Stenosis (Blalock-Taussig, Potts, and Brock Operations): *Records from the Surgical Clinic of Prof. P. Santy.* P. Marion. Lyon chir. 54:254-267 (March) 1958 (In French) [Paris].

The records of the Centre Lyonnais for cardiovascular surgery show that up to July 1, 1957, operations performed on patients with stenosis of the pulmonary artery numbered 386, 350 of which form the basis for this discussion. The mortality was high: 86 (24%) of the patients died, 65 at the hospital within 1 month after the operation and the remaining 21 some months or years later. Chronic anoxia, which usually prompts the operation, is the most frequent cause of peroperative and postoperative failure. Cardiorespiratory syncope, the form under which it appears during the operation, occurred in 18 patients, most of whom were highly cyanotic before the operation. Cerebral anoxia, or cerebral thrombosis, the form in which chronic anoxia manifests itself after operation, may assume various clinical aspects, e. g., coma, or hemiplegia or monoplegia or aphasia with or without coma.

Brock's orificial valvulotomy was performed on 28 patients with pulmonary stenosis without interventricular communication. Four patients died, 1 of peroperative syncope, 1 of thrombosis of the right ventricle, 1, a 52-year-old woman, of cardiorespiratory insufficiency, and 1 of anoxia. This last patient was a nursling who was found at autopsy to have a suborificial stenosis which had not been detected at exploration. Follow-up of the 16 surviving patients with electrocardiographic signs of tight stenosis before operation showed perfect or good late results in 13 and functional failure in 3. There were no late deaths.

The operations used in treating patients with the tetralogy of Fallot with permeable pulmonary stenosis, i. e., the ordinary type, were those of Potts (158), Blalock (95), and Brock (10). The operative risk is greater when the aorta is on the right side. Potts's operation is safer than Blalock's, especially in patients aged less than 1 year or more than 15 years. The late results, however, were about the same (80 to 90% good) for both of these operations. Acute postoperative cardiac insufficiency is exceptional; it was never seen after operations for the tetralogy of Fallot but appeared only in patients with more complex forms of pulmonary stenosis. Infectious endocarditis developed in 6 patients after the Blalock operation, but in only 1 after the Potts operation. The results of the Blalock-Taussig and Potts shunts in patients with rare forms of pulmonary stenosis (extreme tetralogy of Fallot, pseudotruncus arteriosus, and tricuspid atresia) were generally poor. The dimensions of the foramen ovale and the age of the patient seem to be the controlling factors in cases of tricuspid atresia. Patients in whom pulmonary stenosis is accompanied by excessive deviation of the electric axis constitute a special group with a particularly poor operative prognosis, as shown by 14 deaths in 22 cases. The fact that the 8 survivors were much older at the time of the operation than those who died seems to show that the risk diminishes with age and that the operation should not be performed too soon.

Clinical Management of Posttraumatic Rupture of the Thoracic Aorta. B. Eiseman and W. G. Rainer. J. Thoracic Surg. 35:347-358 (March) 1958 [St. Louis].

The authors report on 6 men, between the ages of 20 and 63 years, with rupture of the thoracic aorta due to nonpenetrating trauma. The 1st patient had an aneurysm of the thoracic aorta after a severe injury to the chest sustained in an automobile accident; the aneurysm was located immediately below the left subclavian artery and was followed by chest roentgenograms without evidence of its progression for 16 years. The 2nd patient had a post-traumatic aneurysm which was first observed 2 years after injury and raised the clinical problem of its resection against the advisability of watchful waiting. The latter method was chosen, and the lesion remained unchanged for 4 years. For 9 days after injuries sustained in an automobile accident, the 3rd patient had essentially no symptoms referable to the chest. He was about to be discharged when within an 8-hour period chest pain occurred which was associated with hemothorax. The patient went into shock, and an emergency thoracotomy on the left revealed a ruptured aneurysm of the thoracic aorta which was resected. A nylon graft was inserted, but the patient died shortly after the occluding aortic clamps were removed. After severe injury to the chest, which the 4th patient sustained in a fall from a third-story window during an epileptic seizure, the chest roentgenogram showed widening of the mediastinum. Exploratory thoracotomy revealed diffuse periaortic hematoma, but no evidence of rupture of the aorta was found. Three weeks after the injury and negative exploratory thoracotomy, a chest roentgenogram revealed an aortic aneurysm immediately beneath the left subclavian artery. Thirteen years after chest injury sustained by the 5th patient, an aneurysm of the descending thoracic aorta was thought to be enlarging and producing back and chest pain localized to this region. It was successfully excised and replaced with a homograft, providing relief of symptoms. The 6th patient sustained severe trauma to the left side of the chest at the age of 17 years when he was kicked by a mule. A mass was noted in the descending portion of the aortic arch on a chest roentgenogram taken 38 years after the injury. A follow-up by serial roentgenograms was carried out for 9 years, and marked enlargement of the aneurysm was observed during the last 4 years, 43 years after the injury.

The findings in these patients and observations made by other workers in 95 cases of post-traumatic rupture of the thoracic aorta collected from the literature suggest the following clinical approach. Early thoracotomy should be performed if incomplete laceration of the aorta is seriously suspected. Such a procedure should include careful inspection and palpation of the entire length and circumference of the thoracic aorta for evidence of laceration. Exploratory aortotomy may even be necessary to visualize the site of rupture if no other method discloses the origin of diffuse periaortic ecchymosis. An asymptomatic period of 2 to 3 weeks may elapse after severe injury of the chest before delayed rupture of the aorta occurs. Immediately before the exsanguinating hemorrhage from an incomplete laceration of the aorta or from the resulting aneurysm, there commonly is a short period (1 to 36 hours) of lesser leak. This premonitory warning must be recognized instantly, and immediate thoracotomy must be performed for operative cure. Asymptomatic post-traumatic aneurysms of the thoracic aorta, discovered incidentally more than 1 month after injury, probably will stabilize and can be managed expectantly with serial roentgenograms of the chest at 6-month intervals. Should there be any evidence of enlargement or development of symptoms, the aneurysms should be excised and replaced with a suitable graft.

Primary Extragenital Chorioepithelioma in the Male Mediastinum. G. J. Magovern and B. Blades. J. Thoracic Surg. 35:378-383 (March) 1958 [St. Louis].

The authors report a case of primary extragenital, mediastinal chorioepithelioma in a 20-year-old man who was admitted to the George Washington University Hospital in Washington, D. C., because of a radiopaque shadow in the hilar region on the right, revealed for the first time by a routine chest roentgenogram taken 2 months before admission. The patient was asymptomatic except for occasional pain in the left side of the posterior chest wall. A right-sided thoracotomy was performed, and a large globular, irregular, encapsulated mass was removed from the anterior superior mediastinum. Microscopic examination of the surgical specimen revealed a germinal tumor, the prime elements of which were seminoma and embryonal carcinoma, with areas of choriocarcinoma. Serial sectioning of both testes was negative for germinal tumor but did show azoospermia. Gynecomastia was not present. The remainder of the patient's clinical course was rapidly downhill because of extensive skeletal and retroperitoneal metastasis. He died 5 months after the surgical removal of the tumor.

The case of this patient is believed to be the 25th reported case of primary extragenital chorioepithelioma in a male patient proved by autopsy and serial sectioning of both testes. It is the 10th such case of mediastinal origin. Although extragenital primary tumors have been considered in the past to be the result of aberrations in somatic development, other workers recently have shown by comparative morphogenesis the germinal cell development of extragenital primary tumors as well as of genital primary tumors. While most cases are reported as "extragenital chorioepithelioma," they are, in reality, cases of germinal tumors in which chorioepithelomatous elements have developed, and it is questionable whether these cases should be reported as a distinct entity. The hormonal elaboration, the age of the patients, and the presence of gynecomastia (in 12 of the 24 patients whose cases were collected from the literature) have been briefly discussed and stressed as diagnostic criteria in these patients. The treatment of chorioepithelioma, which is highly radioresistant, consists of radical excision and is extremely unsatisfactory. Most patients die rapidly of metastasis.

Successes and Failures in Homografting of Arteries. D. Erlik. Harefuah 54:113-116 (March 2) 1958 (In Hebrew with English Summary) [Tel Aviv, Israel].

Of the various indications for arterial surgery, the most important are aortic aneurysm, obliteration of the aortic bifurcation (Leriche's syndrome), arteriosclerotic obliteration of the iliac or femoral arteries, and some rare cases of thromboangiitis obliterans (Buerger's disease) in which the obliteration involves the femoral or even the iliac arteries. The exact diagnosis is important, because a deficient outflow below the graft dooms the operation to failure from the start. To obtain an exact picture of the arterial tree, translumbar aortography was used. The procedure was performed on 103 patients by injecting a 70% iodopyracet (Diodrast) solution, with the patient under anesthesia, without a single serious complication. Freeze-dried lyophilized grafts were used. The cases of 10 patients are described in detail. Two of these patients were advanced in years and had aneurysms; they were operated on with good result, as revealed by follow-up for 6 and 15 months respectively. Of 3 patients who underwent aortic resection and received homografts for obliteration of the aortic bifurcation, 1 was a therapeutic failure because of deficient outflow, 1 who was followed up for 6 months obtained excellent results, and 1 obtained good results as revealed by follow-up for 5 months. Homografting of peripheral arteries was carried out in the remaining 5 patients. Relatively short grafts of 20 to 25 cm. in length were used in 3 of these patients, who obtained lasting good results as revealed by follow-up for 13 months. The homografts used in the remaining 2 patients were 42 cm. in length. One patient was a therapeutic failure due to thrombosis. Good results were obtained and maintained for 16 months in the last patient. In general, the shorter the grafts, the better the results. Careful selection of patients and exact technique are the prerequisites for good and lasting results.

Malignant Transformation of Gastric Adenomatous Polypi. D. Rosenberg and J. A. de Mello Saraiva. Rev. paulista med. 52:1-16. (Jan.) 1958 (In Portuguese [São Paulo, Brazil].

Gastric adenomatous polyp is a rare, proliferating, benign tumor prone to undergo malignant degeneration. It is more common in men and in persons between the ages of 60 and 70 years. As a rule, it is asymptomatic, or it may cause symptoms resembling those of gastric or duodenal ulcer, gastric cancer, or other gastric disorders. Pernicious anemia, atrophic gastritis, and massive gastric or rectal hemorrhages are frequent. A diagnosis is made by roentgenologic examination of the stomach and the esophagus and confirmed by gastroscopy. The treatment consists of either polypectomy or gastrectomy, according to the number and size of the polyps.

The subjects of this report were a woman and a man, 37 and 59 years old respectively. The first patient had symptoms of gastroduodenal ulcer. Roentgenologic examination of the stomach showed a round clear image in the antrum. Given a diagnosis of a gastric polyp, an operation was performed on this patient, and a tumor, the size of a hazelnut, was removed. Histological examination of the tumor showed aberrant pancreatic tissue in the gastric mucosa. The patient remained clinically and roentgenologically cured after the operation. The second patient had rapidly lost weight during the 3 months prior to consultation. A clinical, roentgenologic and endoscopic diagnosis of gastric cancer was made. A polyp, 10 cm. in diameter, was found during the operation and was surgically removed. Histopathological examination of the specimen showed an adenomatous polyp. Six months later the patient complained again of a gastric disorder and loss of weight. Roentgenologic examination of the stomach showed a tumor at the site which had been occupied by the first tumor. A gastrectomy with removal of the tumor was performed 1 year after the first operation. The tumor was the size of an orange. Histological examination showed gastric adenocarcinoma. The tumor originally removed had been kept in paraffin and was now histologically reviewed. Sections of the deep layers showed malignancy. The patient died 3 months after the second operation. The authors conclude that polypectomy is indicated only in cases of solitary, small, gastric, adenomatous polyps, no more than 1 cm. in diameter. Gastrectomy with ample removal of the polypous lesion is indicated in all cases of multiple polyps, regardless of their size, and also in cases of a solitary polyp, more than 1 cm. in diameter. The extension of the polypous lesions may in certain cases call for a total gastrectomy.

Sequelae of Total Gastrectomy and their Treatment. O. Rainer and S. Zollner. Arch. klin. Chir. 286:539-553 (No. 6) 1958 (In German) [Berlin].

The authors report on 151 patients who underwent total gastrectomy at the district hospital in Klagenfurt, Austria, and on whom follow-up examinations were carried out in the last 7 years. Three forms of anemia were observed after gastrectomy: (1) anemia of iron deficiency; (2) abnormal composition of the blood of the pernicious anemic type; and (3) anemia of the aregenerative type. An early detection of the anemia of iron deficiency as well as of the masked sideropenia is important, since a cure will be obtained only by the administration of iron. When atrophic changes of the mucosa in the small intestine occur, intravenous treatment with iron becomes necessary. Duration of treatment depends on the iron deficiency as revealed by the capacity of absorption of iron, the normal level of which is about 200 mcg. per 100 cc. of blood. Anemia of iron deficiency with disturbances of absorption by the intestine requires intravenous administration of ferric saccharate. Emphasis is put on the fact that this administration of iron presents an unphysiological method, and consequently it requires control determinations of the capacity of iron absorption after 1,000 mg. of iron have been given. Disturbances of maturation of red blood cells, as evidenced by the presence of megaloblasts, can be prevented by the continued administration of vitamin B_{12}. Only one case of pernicious anemia was observed and that in a patient who discontinued the prophylactic treatment with vitamin B_{12} of his own accord. Reduced fat absorption necessitated greater fat intake at more frequent meals. The disturbed carbohydrate metabolism was examined in patients with the dumping syndrome. Results confirmed the necessity of restricting the carbohydrate, more especially the sugar, intake. A relationship between protein and iron metabolism was shown by the increase in beta globulin level in the serum of patients with iron deficiency. With a greater interval between the gastrectomy and the follow-up examination, the gamma globulin level in the serum increased.

Eosinophilic Granuloma of Bone. H. Hellner. Arch. klin. Chir. 286:564-581 (No. 6) 1958 (In German) [Berlin].

Eosinophilic granuloma has been identified by this term since 1940, but the lesion was known before under several other names. Hellner presents 9 illustrating case histories. In the first 4 cases single foci existed; these were in the ilium in 1 patient, in the humerus in 2 patients, and in the femur in 1 patient. Single cranial foci existed in 3 patients, and the last 2 patients had multiple foci. The patients are usually young, about two-thirds being less than 20 years old. One or more lesions develop rapidly in some part of the skeleton, usually without noticeable symptoms. If the lesion is in the cranium, a bump may appear. Roentgenoscopy reveals a rapidly progressive osteolysis. The cranial lesions usually show no reactive marginal zone, but those in the diaphysis of the long bones are generally oval. The periosteal reactions accompanying the latter lesions often lead to erroneous diagnoses. Most frequently they are mistaken for osteomyelitis, but they have also been mistaken for sarcoma, myeloma, or myelosarcoma. Blood eosinophilia is not always present, but sometimes it is quite marked.

Single foci usually do not recur after surgical removal or roentgen-ray irradiation. Occasionally spontaneous cure takes place. Multiple foci, in the form of "eosinophilic granulomatosis" in young children, may develop into Letterer-Siwe's disease (xanthomatosis). Observations on patients with Hand-Schüller-Christian's disease (xanthomatosis of a cholesterol type) suggested that in some of these it was difficult to make a clinical differentiation from eosinophilic granuloma. The author believes, however, that in the classical form of Hand-Schüller-Christian's disease, with lacuna formation in the cranial vault, exophthalmos, and involvement of the pituitary, the differentiation from eosinophilic granuloma is clear. Today many observers are of the opinion that there are transitional lesions between eosinophilic granuloma and Hand-Schüller-Christian's disease. The author agrees with this on the basis of his own observations. From the clinical point of view it is most important for eosinophilic granuloma, particularly if it appears as a single lesion, to have a favorable prognosis, whereas the prognosis is unfavorable in Letterer-Siwe's disease and is doubtful (20% mortality) in Hand-Schüller-Christian's disease. It remains to be established whether the same causal factor, influenced by the age or reactivity of the patient, may produce these different forms of reticulosis.

Pitfalls and Success in Surgical Treatment of Focal Epilepsy. W. Penfield. Brit. M. J. 1:669-672 (March 22) 1958 [London].

Commenting on the results of surgical therapy of focal epilepsy, Penfield says that the attacks were stopped in 41% of the cases, and the results were regarded as satisfactory in an additional 35%. The mortality has remained in the vicinity of 1.5% for a total of 470 patients. In this report the author is concerned with hazards and pitfalls that the neurosurgeon encounters in the surgery of atrophic epileptogenic lesions. Contrary to an earlier conception, simple adhesions between dura and arachnoid are not to be considered a cause of seizures unless the cortex has been lacerated, so that dural arteries enter the brain through the adhesions to anastomose with intracerebral arteries. If the surface of the brain is exposed for any length of time, it becomes injected, with the rapid appearance of small new vessels, and adhesions will form even if the surface is kept moist. The author believes that the pia becomes inflamed as the result of an exchange between brain and air that can occur through fluid but not through dura mater or membrane. The injection of the pia disappears within a few minutes after pliofilm is laid upon it, provided that it has not been present too long.

Postoperative neuroparalytic edema is the second hazard discussed. It has been a habit to attribute the paralytic and irritative symptoms to edema of the brain. But it is probably more accurate to attribute both the symptoms and the edema to a common cause. The paralytic effect is usually most marked in the immediate vicinity of the cortical excision. Thus, one may expect transient loss of cortical sensibility in the arm after removal of parietal convolutions just posterior to the postcentral gyrus, and paralysis or paresis of the contralateral arm if the excision was located near the precentral gyrus. When the anterior portion of 1 temporal lobe is excised, there is usually transient weakness of the opposite side of the face. If the temporal excision is carried out on the dominant hemisphere, there may well be aphasia which develops about the second day and continues for 2 or 3 weeks. There may be an irritative effect as well as a paralytic one. The author has no idea what the cause of these local seizures may be. He calls them "neighborhood seizures" and expects them to occur perhaps once in 5 operations. They stop in a few days after there has been some increase in the administration of phenobarbitone.

Long-continued temperature elevation for a period of weeks means infection or aseptic meningitis. This latter condition is much more frequent after cortical excision of atrophic lesions in the treatment of focal seizures than it is after craniotomies for other purposes. The cause of aseptic meningitis seems to be the entrance into the subarachnoid spaces of a product derived from blood that has clotted in the wound. In order to prevent this reactive meningitis, it has been the author's practice to close the ventricle if it has been opened. This can be done with 2 or 3 sutures of silk placed in the ependyma, on either side of the opening, and tied loosely over a square of Gelfoam. When aseptic meningitis persists for more than 2 or 3 weeks, it may be wise to reopen the wound and close any fistula that may be present in dura or in ventricular wall. Commenting on the lesion left by excision, the author says that the operative wound does not often ripen into a new epileptogenic lesion. On the other hand, many partial failures must be due to the fact that not all the epileptogenic gray matter has been removed. Sometimes, of course, complete removal is not possible, owing to multiplicity of foci or because the function of the area to be removed is too precious. This is the surgeon's major dilemma. Adequate preoperative electroencephalographic study will keep him from operating on any patient whose focus of epileptic discharge lies in the brain stem. Incomplete removal can be detected by a second electrocorticogram, which may show increased activity of "spike" discharges in neighboring abnormal gyri. So the surgeon removes more of the lesions with the help of the electroencephalographer until at last he hears the welcome words, "All clear, no spikes."

Hemiplegia due to interference with lenticulostriate arteries is the most unsuspected pitfall of all. The author and his associate are preparing a special report on this problem. They believe that sudden paralysis may occur while gray matter is being removed from beneath the branching middle cerebral artery as it passes upward and outward over the insula and over the superior opercula. It seems most likely that some pulling or handling of the artery may cause occlusion of the perforating vessels that enter the perforated space which is situated just beyond. Although some of the 8 patients in whom the author observed this complication have recovered almost completely, he emphasizes that this is the most dangerous area for cortical removal.

Post-Traumatic Renal Insufficiency Without Oliguria. *H. Smitskamp. Nederl. tijdschr. geneesk.* 102:215-220 (Feb. 1) 1958 (In Dutch) [Amsterdam].

Post-traumatic renal insufficiency can develop without an initial period of oliguria. The histories of 2 patients are presented whose urinary output increased to a minimum of 400 ml. in the first 24 hours after the trauma. The urea content of the blood, however, continued to rise, even after the output of urine had reached more than 1,500 ml. in 24 hours. The presence of extensive retroperitoneal and intramuscular hemorrhages, which added to the usual increase of post-traumatic protein catabolism, was regarded as an important contributory factor to the renal insufficiency. The infusion of hypertonic dextrose solution into the vena cava via a polythene catheter, together with rigid fluid control, resulted in rapid improvement and ultimate recovery.

Cutaneous Necrosis Due to Norepinephrine: Analysis of Reported Cases and Surgical Treatment. A. S. Close and W. H. Frackelton. Wisconsin M. J. 57: 127-131 (March) 1958 [Madison].

Levarterenol (l-norepinephrine) is used in various hypotensive states, but its intravenous administration is often followed by ischemic complications. Close and Frackelton collected data on 55 instances of cutaneous necrosis resulting from the administration of levarterenol in 46 patients. The authors tabulate the data on many of these and on 6 of their own patients. To prevent extravasation, cannulas and catheters should be secured by ligatures. The muscular part of the arm should receive preference as the site of administration, because slough is more likely to occur in the lower extremity after prolonged administration, and where extravasation is permitted. Two effective methods for preventing slough are presented: (1) the infiltration of ischemic areas with a saline solution of Regitine and hyaluronidase and (2) administration of levarterenol through a catheter in the iliac vein via a high saphenous phlebostomy.

Ischemic areas that will progress to necrosis have a typical appearance. They are cold, pale, and, if associated with localized extravasation, boggy. They are frequently tender. Since the majority of the patients who receive levarterenol are critically ill, it is wise to delay surgical treatment of the slough until the patient is out of danger. A thick, tough, black eschar usually forms in the area of necrosis and involves all layers of skin. The eschar remains impervious for 2 to 4 weeks, a period sufficient to permit enough improvement in the patient's general condition to warrant definitive treatment. The eschar is then removed at the bedside by sharp dissection. After several days of intermittent moist saline dressings, a thin split-thickness skin graft is removed and applied to the granulation bed with the patient under local anesthesia.

Experiences with the Surgical Treatment of Mitral Stenosis. J. A. Williams, D. Littmann and R. Warren. New England J. Med. 258:623-630 (March 27) 1958 [Boston].

This report is based on a study of 52 patients (51 men and 1 woman) treated surgically for Mitral stenosis in a Veterans Administration hospital during the 5-year period ending in November, 1956. Since almost all the men had been able to pass physical examinations for military service in the not too remote past, it is probable, although not certain, that the valvular disorders in these cases were acquired relatively late in life or were of such minimal degrees as to escape detection. The 47 patients in whom the preoperative diagnosis of mitral stenosis was substantiated at operation are discussed first and are identified as group A. It is generally recognized that mitral disease is statistically less common in males than in females. Observation on these male patients suggested that the clinical patterns of mitral disease tend to be considerably less "typical" in males than in females. The unusual features in this predominantly male material were the frequency of hemoptysis before surgery (70%) and the prevalence of calcific involvement of the mitral-valve leaflets (83%). There were 6 operative deaths among the 47 patients on whom commissurotomy was performed; 3 were due to embolization, and 3 to cardiac failure. Follow-up studies indicated that 2 patients succumbed to recurrent rheumatic carditis and that, of the remaining 39 patients, 35 were benefited by commissurotomy. Improved functional status was usually, but not always, accompanied by reduction in pulmonary hypertension. No patient had recurrence of hemoptysis after surgery. Mention is made of a helpful electrocardiographic sign, the "T mitral," indicative of early hypertrophy of the right ventricle. This pattern consists of an unusually tall and sharp T wave after a wide P wave. It was evident in the tracings of 15 patients, all of whom had important degrees of mitral stenosis. The limitations of catheterization of the right side of the heart in the differential diagnosis of pulmonary hypertension are discussed.

The 5 patients in whom the diagnosis of mitral stenosis was incorrect are designated as group B. Three of these 5 were found to have preponderant mitral incompetence with little or no stenosis. Valvular calcifications, commonly regarded as indicative of mitral stenosis, had been detected fluoroscopically in 1 of these patients before surgery and were found in all 3 at operation. In the other 2 patients in this group, despite extensive studies including catheterization of the right side of the heart, a definite preoperative diagnosis could not be established. Hemoptysis had occurred in both; both were seriously disabled and had auscultatory signs of mitral stenosis. Exploratory cardiotomy revealed no disease of the mitral valve in 1 patient and questionable disease in the other. After operation, each patient continued his preoperative course of progressive disability until death, 18 months and 26 months respectively, after surgery. Autopsy performed on 1 of these patients established "idiopathic cardiomegaly" without anatomic valvular abnormalities or histological evidence of rheumatic heart disease. Although autopsy was not performed on the second patient, diffuse myocardial disease was considered on clinical grounds to be the primary cause of death.

Bacterial and Mycotic Endocarditis Following Cardiac Surgery: Report of a Case. B. H. Hyun, E. A. Dawson and R. E. Pence. J. Thoracic Surg. 35:298-304 (March) 1958 [St. Louis].

The authors report on a 32-year-old man, with a preoperative diagnosis of predominant mitral insufficiency, in whom a total circumferential suture of the mitral ring was accomplished without apparent difficulty. The 5-finger annulus found on internal palpation of the mitral valve was reduced to a 3-finger diameter with favorable pressure changes. The insufficienccy was thought to be improved by 90%. After an uneventful immediate postoperative course, the patient's temperature rose to 104 F (40 C). Escherichia coli was recovered from the urine, and hemolytic Staphylococcus pyogenes var. aureus was recovered from the blood. A diagnosis of acute bacterial endocarditis was made, and penicillin was given by the intravenous route. For 8 days the temperature spiked between 99 F (37.1 C) and 104 F (40 C). From the 5th to the 8th week of hospitalization the temperature never rose above

98.6 F (37 C). Intravenous administration of penicillin was continued for 8 weeks, and then oral administration of penicillin was substituted. In less than 24 hours, chills and fever of 102 F (39 C) recurred. Intravenous administration of larger doses of penicillin was resumed, and at the end of the 9th week the patient's temperature was restored to normal and remained normal from the 10th to the 13th week when intravenous administration of penicillin was again discontinued and oral administration was started. Within 36 hours the patient's temperature once more began spiking and varied between 97 F (36.2 C) and 104.4 F (40.2 C) until death. Hemolytic Staph. pyogenes var. aureus was once more recovered from the blood during this period.

At autopsy a diffuse fibrinous pericarditis was found. A portion of the circumferential suture used to produce reduction in the size of the mitral annulus was found lying free in the left auriculoventricular lumen, having been misplaced at the time of the operation. Microscopically, the thrombotic material from the "purse string" contained colonies of staphylococci. In addition, this thrombotic material also showed extensive mycotic growth. The fungi, identified as Candida albicans, were arranged in a foliate pattern, showing septate myceliums and yeast-like cells. Fourteen cases of bacterial endocarditis after cardiac surgery were collected from the literature. Thus, while not a common complication, it occurs with sufficient frequency that it must be regarded as 1 of the hazards of such surgical intervention. In most of the cases hemolytic Staphylococcus organisms were the pathogenic agents.

Late Results of Direct Surgery of the Aortic Bifurcation and Its Major Branches. F. B. Cockett and A. G. Norman. Brit. M. J. 1:727-734 (March 29) 1958 [London].

A detailed follow-up study of 30 patients treated at St. Thomas's Hospital in London for either arteriosclerotic occlusion or aneurysm of the abdominal aorta and its major branches, who underwent direct arterial surgery during the last 5 years, is presented by the authors. Three different types of direct arterial surgery have been used: (1) replacement with stored homograft; (2) replacement with plastic prosthesis; and (3) endarterectomy or "rebore" of the occluded segment. Of 18 patients on whom replacement with stored homograft was performed, 2 died in the early postoperative period as a direct result of the operation, probably due to sepsis in the graft which resulted in late leakage and rupture of an anastomosis. Of the remaining 16 patients, there was a serious complication resulting in loss of a limb in 3 patients. Thirteen patients have had success in varying degree, and 10 of these obtained good results. As to the technique of inserting grafts, the end-to-side type of arterial anastomosis has proved superior over the end-to-end type. In fact, in the whole series there has not yet been a case of delayed occlusion of an end-to-side type of anastomosis. Of 6 patients on whom plastic prosthesis was performed, 2 had aortic thrombosis and 4 had an aneurysm of the aorta. One patient in each of these two groups died. The use of the polyvinyl sponge prosthesis was unsatisfactory in both patients with aortic thrombosis. Of the 4 patients with aneurysm, the 3 surviving patients obtained highly satisfactory results from replacement with Orlon tubes. The latter material may be preferred to the polyvinyl sponge. These findings suggest that in patients with arteriosclerotic thrombosis plastic material is unsatisfactory, while it is suitable in those who require a short-segment replacement of a large vessel such as the dilated aneurysmal aorta. The results were most encouraging in 6 patients on whom removal of an obstructing thrombus had been performed by way of "disobliteration" or "rebore." There were no deaths, there have been no major complications, and the follow-up results to date have been satisfactory. With improvements in the technique of "rebore," the authors believe that the indications for this type of operation can be considerably extended.

Coronary disease and cerebral thrombosis occurred in only 1 of the 20 patients who were under 60 years of age; only 4 (40%) of the 10 patients over 60 years of age had coronary disease. On the basis of these results surgical treatment is recommended for any patient in the under-60 age group with arterial occlusion. If the lesion is a localized occlusion with reasonably good artery on either side, direct removal of the occluding thrombus from the artery—"rebore"—is a sound and safe operation. If the arterial disease is more widespread, a better long-term result will be obtained by radical resection of the whole aortic bifurcation and bypassing the diseased segments on each side with a stored homograft. In the over-60 group one's attitude is tempered by the increased likelihood of other arteriosclerotic lesions such as angina. However, the benefits of this type of surgery far outweigh the risks.

The Surgical Therapy of Occlusive Coronary Artery Disease—Present Status. A. A. Bakst and L. Loewe. Am. J. Cardiol. 1:340-344 (March) 1958 [New York].

In an attempt to evaluate various surgical procedures designed to correct coronary artery disease by augmenting the extracoronary arterial collateral circulation, 2 physiological tests were performed on animals. The peripheral segment of the ligated circumflex coronary artery was cannulated, and a continuous flow of arterialized blood was obtained. This flow served as a measure of intercoronary collateral circulation. Next, perfusion experiments were performed. With the heart of the animal in situ, the ascending aorta was clamped distal to the orifices of the coronary arteries. The descending aorta was cannulated, and the arch and the descending aorta were perfused with a neoprene latex solution at a pressure of 160 to 180 mm. Hg. Under these conditions, any material found within the coronary arteries could not have entered through their normal ostiums and must have arisen from extracoronary circulation.

The surgical procedures assessed in animals by these physiological tests were pericardial poudrage as described by Thompson, deepicardialization, i. e., a modification of pericardial poudrage as described by Harken and co-workers, and implantation of the internal mammary artery as described by Vineberg. Poudrage seemed effectively to fill the circumflex coronary artery in 50% of the animals. Implantation of the internal mammary artery showed good filling of the anterior part of the descending artery in 90% of the specimens and of the circumflex coronary arterial tree in 25%. It, therefore, seems that each of these procedures is effective in producing extracoronary collateral circulation to a segment of the coronary arterial tree. The authors' present concept has matured to a combination of pericardial poudrage and implantation of the internal mammary artery to protect both the anterior and the posterolateral portions of the left ventricle against coronary artery occlusion. This consists of the implantation of the internal mammary artery into the anterior wall of the left ventricle, combined with the instillation of magnesium silicate posteriorly and posterolaterally over the wall of the left ventricle. The modification of the Vineberg technique by performing it through an anterior approach not only facilitates the dissection of the vessel but also permits the patient to be placed in the supine position which is best tolerated by the cardiac.

Bronchography in Pulmonary Tuberculosis: Studies on Its Value in Patients Being Considered for Surgery. D. L. Merrill and P. C. Samson. Am. Rev. Tuberc. 77:561-592 (April) 1958 [New York].

One hundred thirty-one bronchograms were obtained from 105 patients who were admitted to the thoracic surgery service of the Highland-Alameda County Hospital in Oakland, Calif., during the year 1956. Of the 105 patients, 38 had proved tuberculosis and 5 were suspected of having tuberculosis. Repeat bronchograms were obtained from 10 of the 38 patients for observation of the course of the disease. Twenty-nine of the 38 patients had not received previous surgical treatment, and 9 had been operated on previously. The contrast medium used was Dionosil (3,5-diiodo-4-pyridone N-acetic acid); it proved to be useful because of its low viscosity, prompt absorption, and rapid excretion; it uniformly allowed visualization of the segmental bronchi and bronchioles, which was of considerable diagnostic value.

Bronchographic observations made in the 43 patients with proved or suspected tuberculosis and in those reported on by other workers seem to justify the following general conclusions. Bronchiectasis with terminal bronchostenosis of the segmental bronchus is usually the concurrent and early end-result of advanced parenchymal disease or of tuberculous endobronchitis. With such a bronchographic finding, the question of persistent disease and of the viability of "nonculturable" tubercle bacilli becomes much more acute; the incidence of recurrence may be considered sufficiently high to warrant resection. This holds equally true for "initial" as for "retreatment" patients. Bronchiectasis in patients with tuberculosis is evidence of previous or currently active disease in the segment involved. In the absence of terminal segmental stenosis, there is usually bronchiolar filling which indicates functioning lung with minimal disease. Whether these segments should be removed is questionable. The value of resecting or preserving such segments must be weighed according to the extent of other areas of involvement, the problems of postoperative space management, the susceptibility of the patient's tubercle bacilli to the available chemotherapeutic agents, and the patient's clinical course. At the present time the authors are not resecting additional segments on the bronchographic evidence of associated bronchiectasis alone.

Saccular bronchiectasis (either nonspecific or tuberculous), especially of the apical regions of the lung, is often the late result of chronic fibroid tuberculosis and may represent a source of infectious sputum or of recurrent hemoptysis, especially in older patients. Such lesions may require surgical treatment. The demonstration of cavities by direct filling with the bronchographic agent is sporadic and unreliable. Bronchography is of proved value in the diagnosis and evaluation of major bronchial disease associated with adjacent lymphadenopathy. Bronchography has considerable screening value in patients with recurrent or progressive clinical disease after previous surgical intervention. Unsuspected empyema spaces with bronchial communication (occult fistula) and the differentiation of such lesions from cavities involving the superior segment of the lower lobe or other areas are often possible with Dionosil. Bronchography has also proved useful in evaluating the effect of surgical intervention in selected cases, such as symptomatic bronchial torsion occurring after segmentectomy.

Bronchography is indicated before almost any surgical approach to the treatment of pulmonary tuberculosis. The preoperative delineation of anatomic and architectural anomalies, the finding of lobar, segmental, or subsegmental involvement (especially in contracted areas of the lung), and the occasional observation of an unsuspected, but frequently significant, condition, such as a spontaneous bronchopleural fistula or nontuberculous basilar bronchiectasis, may be apparent with no other diagnostic technique. Bronchographic findings in patients with pulmonary tuberculosis are informative and of value in planning resective surgery, especially in patients with drug-resistant infections, in the management of residual lesions, and in the evaluation of residual disease after previous surgical intervention.

Vitallium Tube Method for Repair of Strictures of the Bile Ducts. D. W. McGoon and O. T. Clagett. Surg. Gynec. & Obst. 106:409-412 (April) 1958 [Chicago].

The authors describe experience with the Vitallium tube method of repair of the biliary ducts at the Mayo Clinic since its first application in 1944. All 52 patients who have had a Vitallium tube inserted into the biliary ducts during the repair of strictures of those ducts and reestablishment of end-to-end continuity are included in this study. Adequate follow-up information to October, 1956, was available on all but 4 of the 52 patients. Previous operations on the biliary tract appeared to mark the onset of the stenosis in every instance except 1, and it is assumed that injury to the ducts at operation caused the stenosis. The 1 exception was a 16-year-old boy who sustained injury to the biliary ducts from a bullet that penetrated this region. The operation in which the Vitallium tube was inserted occurred from 2 months to 13 years after the surgical procedure that appeared to have caused the stricture, but most commonly 6 to 18 months had elapsed.

Originally, it was hoped that the Vitallium tube, situated within the biliary duct at the site of the stricture, would remain in place and continue to function indefinitely. A number of these patients returned with recurrent biliary obstruction, and removal of their heavily encrusted and occluded Vitallium tubes became necessary. The operation for the insertion of the Vitallium tube resulted in 1 death; this patient was a very ill women who had had 4 previous attempts at surgical correction of her stricture during the preceding 6 years. She died in a hepatic coma 10 days after the operation. One other patient died of "nephritis and uremia" 9 days after removal of the Vitallium tube elsewhere. The results in 7 of the 48 patients are classified as indeterminate. In 2 of these, removal of the Vitallium tube occurred less than 1 year ago, and although these patients have been doing well thus far, the final result cannot yet be safely estimated. The surgical treatment of the other 5 patients deviated from the scheme outlined in that additional and probably unnecessary procedures were performed at the time of removal of the Vitallium tubes, thus obscuring the final result of the operation as it is now conceived.

The Vitallium tubes have never been removed from 15 patients. Two of these patients have died of causes unrelated to their hepatic and biliary systems. The shortest interval since insertion of these tubes is 14 months. Seven patients still have their Vitallium tubes in place and functioning satisfactorily 11 or more years after insertion. Twelve patients have remained well after removal of the Vitallium tubes. The remaining 14 patients must be regarded as representing failures of the method if critically studied, although 3 of these patients have had a satisfactory result after a second trial of the Vitallium tube method of repair. Only after exploration of the region of the biliary ducts is a decision for or against employment of the Vitallium tube method made. The authors feel that the Vitallium tube is a highly effective method of treating patients with biliary strictures in whom there is no upper remnant of duct extending beyond the scarred undersurface of the liver.

Peripheral Arterial Emboli. W. C. McGarity, W. D. Logan Jr. and F. W. Cooper Jr. Surg. Gynec. & Obst. 106:399-408 (April) 1958 [Chicago].

The authors review observations on 64 patients who had a total of 86 peripheral arterial emboli. These patients were treated at 3 hospitals during the 10-year period from 1946 to 1956. There were 40 males and 24 females. The youngest patient was 13 years old, and the oldest was 87. All but 13 patients were between 40 and 80 years of age, and the peak incidence was in patients between 50 and 70. The authors also review the literature analyzing 2,088 cases and 1,167 embolectomies. Mural thrombi formed on the left side of the heart account for most of the peripheral arterial emboli. Rheumatic heart disease and heart disease after myocardial infarction are the most common causes. A mural thrombus forms within the lumen of the left side of the heart during arrhythmia or after injury to the heart wall and then dislodges to settle elsewhere. Frequently, the patient's history shows that changes have been made recently in his medical treatment or that there has been an alteration in his pulse rate or heart rhythm.

More than 40% of the 86 emboli in the authors' series occurred in the femoral vessel. Vessels of the upper extremities accounted for 18.6%. These percentages are in close agreement with those derived from a review of 2,088 peripheral arterial emboli reported in the literature. Any embolus may be 1 of a series or 1 of several occurring simultaneously. Sixteen of the 64 patients had more than 1 embolus. Auricular fibrillation and myocardial infarction were responsible for the majority of these multiple emboli. Pain or paresthesia at the site of the lesion or distal to it constitutes the most frequent initial symptom of arterial embolus. Treatment of arterial embolus is a medical emergency. The ultimate outcome depends largely upon early recognition and treatment. Not every patient with an arterial embolus is a candidate for embolectomy. Conservative treatment is indicated (1) for patients so critically ill from other diseases or from simultaneous cerebral or visceral embolism that any but supportive treatment may be hazardous and (2) for patients with adequate collateral circulation in the affected extremity. In these patients, sympathetic blocks should be administered immediately to relieve the reflex spasm of the collateral vessels.

In the 64 patients the most frequent site of occurrence was at the bifurcation of the common femoral artery. The best results were obtained when treatment was started within the first 6 to 12 hours after occurrence of the embolus. Seventy per cent of the embolectomies in the series presented by the authors were successful as compared with 38% of the 1,167 embolectomies for which results were given in the reviewed literature. The mortality rate in the 64 patients was 29.6% (12 or 18.7% in the surgically treated group and 7 or 10.9% in the conservatively treated group). Most of the deaths were due to associated diseases. When an embolus lodges in the popliteal vessel or in an artery of the upper extremity, the choice of treatment should be based on the specific findings in each case. When an embolus involves the aorta or the iliac or femoral arteries, it should be treated as a surgical emergency, provided that the patient's condition will permit.

Experience with Triethylene Melamine (TEM) and Triethylene Thiophosphoramide (ThioTEPA) in Recurrent or Metastatic Solid Tumors. R. F. Schell. Surg. Gynec. & Obst. 106:459-465 (April) 1957 [Chicago].

The authors report their experience with triethylene melamine (TEM) and triethylene thiophosphoramide (ThioTEPA, TSPA) in 40 patients with advanced, "hopeless" cases of carcinoma in whom all curative and all established palliative measures had failed or were contraindicated. The purpose of instituting treatment in these advanced cases was twofold: (1) to determine whether these agents significantly inhibited tumor growth and (2) to attempt to make the patient's final remaining days as comfortable as possible. The treatments did not ordinarily impose a severe burden on the patient's financial or physiological economy, and in many cases gave a great psychological "lift" by offering some relief to an intolerable situation. ThioTEPA was given as an injection of a solution containing 10 to 20 mg. per cubic centimeter either intramuscularly for general effect, or into serous cavities to attempt to control malignant effusions, or directly into tumor masses. TEM may also be utilized in a variety of ways and has the advantage of being effective when given by mouth. In this series it was utilized most frequently by being instilled into a serous cavity in a dosage of 5 to 10 mg. Subsequent therapy consisted of the oral administration of the drug in divided doses of 2 to 5 mg. a week, given with bicarbonate of soda one-half to 1 hour before breakfast to lessen gastric irritation and to promote absorption. Occasionally TEM was given by intramuscular injection or by direct injection into tumor masses.

A clinical response was obtained in several cases of adenocarcinoma, particularly those primary in the breast, by systemic therapy with ThioTEPA or the injection of this agent directly into tumor masses. TEM appears to be preferable to ThioTEPA in the control of malignant effusions. No effect from either of these agents was seen in squamous-cell tumors or in mesenchymal tumors arising in organs other than the lymphatic system. The depressant effect of these agents on the bone marrow was the chief cause of complications. In selected cases the use of the antitumor compounds, TEM and ThioTEPA, has been of assistance in easing the distress of terminal cancer cases. It has occurred to several workers in this field that the prophylactic administration of carcinocidal agents at the time of surgery to render the soil less fertile for the implantation of cancer cells could well be helpful. This procedure was started by the author on a limited scale with the use of a single intramuscular or intravenous dose of ThioTEPA immediately after surgery for carcinoma of the breast, and the intraperitoneal administration of TEM after extirpative surgery for abdominal cancers.

A Ten Year Study on Wound Infections. P. Dineen and C. Pearce. Surg. Gynec. & Obst. 106:453-458 (April) 1958 [Chicago].

The records of the New York Hospital-Cornell Medical Center were studied to find patients with wound infections, occurring between Jan. 1, 1947, and Dec. 31, 1956, on the general surgical service and surgical specialties. There was a total of 511 wound infections during this period. These form the basis of this study. Wound cultures were inoculated for primary isolation both aerobically on blood agar plates and in 3% beef infusion broth, and anaerobically in liver dextrose broth. Recently, since the establishment of the surgical bacteriology laboratory, staphylococci have been characterized by mannitol fermentation, coagulase production, antimicrobial susceptibility profile, and phage typing as well as by the production of hemolysin and pigment. Drug sensitivity tests were not done except by the disk method, and in the earlier years of this study these were carried out only upon request. Analyses were made of yearly and monthly incidence, surgical service involved, and species of organisms involved. The rate of infections varied from 0.8 to 1.4% with an over-all rate of 1%.

Infections that occur in the postoperative state are in the great majority of instances caused either by staphylococci or by one or more of the enteric flora. The incidence of wounds infected with intestinal flora has not appreciably changed in the past 10 years, and the seasonal curve does not indicate any significant variation. Because more wounds are infected with staphylococci and in view of the current intense interest in this problem, the present survey was made. Fluctuations in the annual number of infections are comprised almost exclusively of staphylococcic infections. Peak months for staphylococcic wounds in this center are March and December. These peak months of wound infections coincide with the peak months of upper respiratory tract infections. Nasal cultures from 5 surgeons doing most of the major surgery showed them to have coagulase-positive, penicillin-resistant Staph. aureus present during March and April of 1957. In March there were 10 staphylococcic wound infections and in April none. Therefore, it is apparent that the mere carrying of staphylococci does not cause wound infection. Wound infections are usually caused by breaks in technique, a weakened host resistance, or by "persistent" organisms. Increased vigilance on the part of the professional staff is probably the single most important factor in prophylaxis. Attention should also be directed to adequate face masks, to operating-room ventilation, and to the prevention of the "carrier state" by the patient and the professional staff.

NEUROLOGY & PSYCHIATRY

Neurosis Tarda and Heart Infarct. F. J. Tolsma. Nederl. tijdschr. geneesk. **102**:322-325 (Feb. 15) 1958 (In Dutch) [Amsterdam].

The author employs the term "neurosis tarda" when a neurotic syndrome appears in a patient over 40 years of age. He observed 8 patients in whom this was the case after an unrecognized heart infarct. The history of these patients gave no indication of a hereditary tendency or of clinical symptoms of a neurosis. The case records of 5 of these patients are given. They complained of being easily fatigued and showed signs of nervousness and anxiety. Electrocardiographic examination revealed in all the signs of an old heart infarct. It is also noteworthy that none of these patients showed signs indicating the existence of arteriosclerosis. There was a change in character accompanied by psychoneurotic manifestations which took the form of anxiety neurosis, neurasthenia, or hysteriform symptoms. Explaining to the patient that he has had a mild heart attack and suitable psychotherapy are the most important therapeutic measures. Some restriction in physical activity may also be necessary; this will depend on the physical as well as on the psychological status of the patient.

New Method of Phenobarbitone Administration in the Treatment of Epilepsy. D. C. J. O'Connor. Lancet 1:609-611 (March 22) 1958 [London].

O'Connor believes that changing blood levels of phenobarbital explain why preparations of phenobarbital now in common use are not completely successful, toxic effects being caused when the level is high and fits appearing when it is low. He tried a preparation which releases phenobarbital slowly over a long period and which might be expected to produce a more constant blood level. He reports results in epileptic patients in whose treatment phenobarbital "spansules" were substituted for the same drug taken in the form of tablets or solution. Each spansule contained 1½ grains (0.1 Gm.) of phenobarbital in coated granules, which released the drug at a uniform rate, ensuring a steady absorption over a long period. The 18 psychotic, epileptic patients in whom phenobarbital spansules were used had had convulsions and psychoses for more than 10 years. They were examined every 4 months as inpatients and were followed up throughout 1955, 1956, and 1957. The same nurses attended the patients, and the same scheme of interpreting and recording convulsions was followed over the 3 years. The epilepsy was classified as dementia paralytica with major and minor convulsions in 1 patient, post-traumatic Jacksonian epilepsy in 1, idiopathic petit mal in 2, post-traumatic grand mal in 1, and idiopathic grand mal in 13, with hysterical overlay in 1 and periods of status epilepticus in 1.

These patients had the severest form of epilepsy, both in the psychosis and in the frequency and severity of convulsions. The patients were investigated by means of frequent blood and urine studies, chest and skull roentgenograms, and complete physical and neurological examination, with particular attention to tests of speech, walking, and muscular coordination and balance. Before the changeover, the mean daily dose of phenobarbital in the 13 patients receiving it was 2.8 grains (0.18 Gm.); with spansules the mean daily dose in the 18 patients was 5.8 grains (0.37 Gm.). In a few of the patients with severe epilepsy, up to 5 spansules (7½ grains [0.5 Gm.]) were given daily with no ill-effects. The reduction in the number of convulsions, both major and minor, was gradual and progressive after the changeover to phenobarbital spansules. In the 6 months before their introduction the group of 18 epileptic patients had a total of 385 convulsions; in the last 6 months of treatment with spansules the total was 7. The personality and mental state improved in most cases, and toxicity was much reduced. The good effects and low toxicity are attributed to the constancy of the blood barbiturate level that was attained.

Treatment of Homosexuality by Individual and Group Psychotherapy. S. B. Hadden. Am. J. Psychiat. 114:810-815 (March) 1958 [Baltimore].

The author reports a few impressions gained from the individual treatment of homosexuals over almost 30 years, from their treatment in groups with other neurotics, and from their progress in groups made up exclusively of homosexuals. In selecting these patients, only males were included who have persistently and consistently in adult life preferred sexual experiences with those of the same sex and who have had some degree of rejection or revulsion toward sexual union with females. When 3 such patients were forced into private treatment almost at the same time, an opportunity presented itself to initiate a psychotherapy group made up exclusively of active homosexuals. After several preliminary individual sessions, the group was started. Two of the members were 22 years old; the third was 19 years old. The 2 older patients had been active homosexually for over 5 years; the youngest member had had an active homosexual career from the age of 12. At the first session the author learned that all 3 patients were casually acquainted and had often seen each other in homosexual haunts. Their feelings about homosexuality were initially explored. As consideration of their activities progressed, the front-page story of the murder and dismemberment of a sailor by a homosexual known to all 3 of them was discussed. The group sought an explanation of why homosexuals committed such violent crimes, and when it was suggested that only they could supply the answers after examination of their own feelings, anxiety mounted as they disclosed violent emotions activated by threats of exposure and blackmail. Before the first session ended, they were in agreement that homosexuals were not as gentle and artistic as they appeared. At this and several subsequent group meetings not only were murders among homosexuals discussed but their frequent suicides as well. The group's various fantasies in relation to homosexuality were explored, as were the unsatisfactory parental relationships, the disturbed nature of identification with their own sex, and the factors which led to arrest of their psychosexual development. At no time in this and in a second exclusively male homosexual group of 7 members was any attention focused on the nature of their homosexual experiences or the frequency of indulgence. The lack of prying on the part of the therapist is necessary to provide a beneficial experience to all patients.

In such groups the rationalization that homosexualty is a pattern of life the patients wish to follow is destroyed by their fellow homosexuals. This breaking down of their rationalization activates anxiety, and a desire to change is created. Obvious ego-strength is gained by identification with others who are also seeking socially acceptable goals. Identification with a group that has a healthy motivation soon banishes the feelings of isolation from which they suffer. When members reach the point where their homosexual drives have diminished or disappeared and they must completely reject all homosexual identifications and identify with heterosexuality, they are aided in final commitment by fellow members. This result is in contrast to patients in individual treatment, who may discontinue because they cannot make the final commitment; they develop anxiety about the loneliness which may result from giving up their homosexual connections and reach a critical point at which there is likelihood of regression. The group treatment convinces its members that their homosexuality is not an affliction or trick of fate but a pattern of inadequate behavior which can be changed.

Vaccination Against Poliomyelitis: Its Present and Future Status. L. L. Coriell. A. M. A. J. Dis. Child. 95:349-358 (April) 1958 [Chicago].

Three years of increasingly widespread use of killed poliomyelitis vaccine have coincided with marked reduction in reported cases of poliomyelitis. A particularly low incidence and a low-paralytic rate are the otustanding features of the 1957 season. Up to Nov. 15, there had been 1,988 cases of paralytic poliomyelitis reported for 1957, compared with 6,196 for the same period in 1956 and 9,796 for 1955. The decrease in 1957 occurred in all age groups, with a relatively greater proportion of cases occurring in patients from birth to 4 years of age. Estimates suggest that protection against paralytic disease approached 90% in patients who had received 3 or more properly spaced injections of vaccine. About 28 million of the 109 million persons aged less than 40 years have received a full course of 3 injections of vaccine. At least 17 strains of Coxsackie or enteric cytopathogenic human orphan (ECHO) viruses can cause a clinical disease resembling nonparalytic or occasionally paralytic poliomyelitis. These infections have almost certainly been called poliomyelitis in the past. Further research will show how many of the vaccine failures are infections caused by one of these other viruses.

The vaccine is safe, at the sacrifice of some potency. Suggestions for further research to improve potency are (1) disproportionate mixing of the 3 virus fluids in making the vaccine, (2) increasing the potency requirements, and (3) selection of new strains of virus. Such changes take time, and a more potent vaccine will probably not be available before the next poliomyelitis season. In the meantime, one must use the vaccine which is at hand, and the immediate objective should be to complete 3 properly spaced infections for all persons less than 40 years of age. The use of vaccine during 2 epidemics in 1955 and 1956 did not show any beneficial effect on the course of the epidemic. This emphasizes the importance of doing vaccination ahead of time, and all physicians are urged to cooperate by completing immunizations.

On the basis of the data now available, a 4th injection of vaccine is indicated in the spring of 1958, just before the next poliomyelitis season. This is based on the following observations: 1. Although the vaccine is safe and effective, some paralytic cases continue to occur in triple-vaccinated children. 2. Protection appears to be proportioned to the amount of antigen injected. 3. Many children have received incomplete series, improperly spaced injections, or vaccine of poor potency. 4. There seem to be remarkably few reactions or contraindications to the vaccine. This proposed 4th injection is viewed not as a booster but rather as a method for completion of the primary immunization of those who for one reason or another failed to develop an immunological response to previous injections. The actual need for booster shots after this primary immunological response has not been demonstrated and may not be necessary at all after the population is once immunized, except perhaps in infancy and early childhood. At any rate, decision on a permanent plan for future booster shots should certainly be deferred pending more research.

GYNECOLOGY & OBSTETRICS

Treatment of Vaginitis Due to Trichomonas Vaginalis with 2-Acetylamino-5-Nitrothiazole. P. E. Bertoli. Minerva ginec. 9:1006-1010 (Dec. 31) 1957 (In Italian) [Turin, Italy].

Topical therapy of vaginitis due to Trichomonas vaginalis affords only a temporary remission of symptoms, which is followed by endogenous reinfection. The author administered an Italian proprietary preparation, Tritheon (2-acetylamino-5-nitrothiazole-Trichoman), to 2 groups of patients with this form of vaginitis. The first group was treated orally, and the second with a combined topical and oral administration of the drug. The first group, consisting of 23 women, received Tritheon in daily dosage of 300 mg. for 8 days. The patients were reexamined for the presence of T. vaginalis 3 times after the discontinuance of therapy. At the first examination 13 women (56%) had no clinical symptoms of the disease. The second course of treatment brought about complete remission of symptoms in 6 of the remaining 10 women (60%) who had still been positive for the protozoan at the first post-treatment examination. In addition, specimens of spermatic fluid were obtained from 11 husbands of the patients. Six of them, who were infected with T. vaginalis, received Tritheon in daily dosage of 300 mg. for 20 days. The therapy was effective in 5 men.

Better results were obtained with the combined therapy which was given to 25 women in the second group. These patients received Tritheon in daily dosage of 800 mg. divided into 300 mg. given orally and 500 mg. given topically. The first course of treatment brought about complete remission of symptoms in 18 patients (72%). The second course of treatment resulted in complete remission of symptoms in 5 of the remaining 7 patients (71%) who were still infected at the end of the first course. The drug was well tolerated and the author recommends its prolonged use in the management of vaginitis due to T. vaginalis.

Ovarian Function After Combined Surgical and Radiologic Treatment of Early Cervical Cancer. C. Krebs and N. Blixenkrone-Møller. Acta radiol. 49:128-136 (Feb.) 1958 (In English) [Stockholm].

In 18 women, between the ages of 22 and 37 years, with cancer of the uterine cervix, who were given irradiation treatment, an attempt was made to protect the ovaries against the irradiation effect by moving them, before irradiation, from their normal site in the small pelvis and fixing them as far away from the irradiated field as possible without impairing the blood supply. Nine of the 18 patients had cancer of the uterine cervix in stage 1, 6 had cancer of the uterine cervix in stage 2, and 3 had cervical cancer in stage 3. An inferior midline laparatomy was performed. The ligament of the ovary was divided and the ovary with the infundibulopelvic ligament mobilized, care being taken that the blood vessels of the ovary were left intact. The ovary was then lifted up and fixed with silk-knot sutures to the margins of a small incision into the parietal peritoneum on the psoas muscle or retroperitoneally to this muscle, so that the ovary occupied a position above the linea terminalis of the pelvis. The distance between the cancer of the vaginal portion of the uterine cervix and the lower pole of the ovary was usually 13 to 15 cm., and in a few patients up to 18 cm. The oviduct was removed only in exceptional cases, generally if it presented signs of chronic inflammation. Unilateral lifting of the ovary was performed in 7 patients, and bilateral lifting was done in the remaining 11. Five to 8 days after the operation, radium therapy or combined radium-and-roentgen therapy was instituted. The beam of roentgen rays was, as far as possible, directed downwards, away from the new site of the ovaries.

The 18 patients were followed for 6 to 7 years. Of the 9 patients with cancer of the uterine cervix in stage 1, 8 were alive without signs of recurrence after 6½ years and 1 died of recurrent cancer 12 months after the treatment; of the 6 patients with stage 2 cancer, 4 were alive and well without any signs of recurrence; and 1 of the 3 patients with stage 3 cancer was alive and well after 6½ years. Of the 13 surviving patients, 8 had received radium therapy alone and 5 had received combined radium-and-roentgen therapy. Menstrual function was preserved in 6 of the 8 patients who had been given radium therapy alone. Six years after the treatment 1 of the 6 patients became pregnant but had an abortion at the 4th month. Menstrual function was not preserved in any of the 5 patients who had received combined irradiation therapy. These data suggest that neither the lifting of the ovaries nor the preserved ovarian function has aggravated the prognosis of patients with cancer of the uterine cervix, and that it is possible to avoid premature menopause induced by the irradiation therapy in most of the young women with early cervical cancer who can be treated with radium alone.

Pregnancy After Pneumonectomy on Account of Pulmonary Tuberculosis. C. D. Laros. Nederl. tijdschr. geneesk. 102:264-268 (Feb. 8) 1958 (In Dutch) [Amsterdam].

The author attempted to obtain information regarding the course of pregnancy in women who had undergone pneumonectomy for pulmonary tuberculosis. He was able to collect information on 64 women who had had a total of 74 pregnancies after this operation. Seventy of the pregnancies resulted in the birth of healthy children. Three of the 4 stillbirths occurred in the same woman. A connection with the maternal tuberculosis was established in none of the 4 stillbirths. In general, no adverse effect of the pneumonectomy was observed during pregnancy or labor.

PEDIATRICS

Progression of Amaurotic Family Idiocy as Reflected by Serum and Cerebrospinal Fluid Changes. S. M. Aronson, A. Saifer, A. Kanof and B. W. Volk. Am. J. Med. 24:390-401 (March) 1958 [New York].

The authors performed serial biochemical studies on 19 consecutive patients with amaurotic family idiocy, 1 patient with lipid histiocytosis of phosphatide type (Niemann-Pick disease), and 1 patient with diffuse sclerosis. There were 8 boys and 11 girls with amaurotic family idiocy, and their ages at the onset of the disease ranged from 4 to 9 months. Twelve of the children died, and autopsy was performed on 10. The clinical diagnosis in the 19 patients was based on the collective presence of apathy, progressing weakness, amaurosis, arrested development, emergency of abnormal movements, hypersensitivity to sound, and macular degeneration. The children were all of Jewish extraction. The patient with Niemann-Pick disease, a boy aged 5 months at the onset of the disease, and the patient with diffuse sclerosis, a girl aged 6 years and 3 months, are alive. An attempt was made to equate certain consistent changes in the serum and the cerebrospinal fluid with the clinical and the pathological course of the 3 disorders in the 21 patients.

The serum aldolase level, initially normal in the early phase of amaurotic family idiocy, became significantly elevated after about 9 months of clinically evident illness, coincident with the emergence of skeletal muscle atrophy. The latter was believed to be caused by the observed acceleration of lower motor neuron breakdown. In the protracted phase of amaurotic family idiocy, the serum aldolase level generally regressed to normal values. A roughly similar pattern was observed in the patient with Niemann-Pick disease, which is a disorder presenting a central nervous system anatomic component almost identical with amaurotic family idiocy. No comparable changes in serum aldolase level were seen in the patient with diffuse sclerosis or other long tract or upper motor neuron diseases studied.

The serum glutamic-oxalacetic transaminase level was consistently and markedly elevated during the entire course of the disease in all patients with amaurotic family idiocy and in the patient with Niemann-Pick disease. The hypertransaminasemia tended to lessen during the protracted phase of these disorders. In contrast, the girl with diffuse sclerosis (and patients with other neurological disorders) showed normal or minimally elevated values. High transaminase levels were also noted in the cerebrospinal fluid of the patients with amaurotic family idiocy and Niemann-Pick disease. The cerebrospinal fluid transaminase level was depressed in the patient with diffuse sclerosis. These data indicate that the extensive and continuing ganglionic disintegration of amaurotic family idiocy is sensitively mirrored by elevated transaminase levels in the serum and in the cerebrospinal fluid.

The level of total serum neuraminic acid was nonspecifically elevated in the 3 neurological disorders principally studied, in contradistinction to the singular elevation of this substance in the cerebral tissues in amaurotic family idiocy. However, the serum protein-linkage distribution of this substance in these 3 diseases showed a distinctly abnormal pattern, as indicated by the ratios formed by globulin neuraminic acid/total neuraminic acid and globulin neuraminic acid/globulin protein. A significant depression of serum and cerebrospinal gamma globulin levels also was observed in the patients with amaurotic family idiocy. The evidence presented seems to indicate the possibility that the pathophysiological substrate of amaurotic family idiocy may extend beyond the confines of ganglionic degeneration.

Relapses of Tuberculous Meningitis in Children. V. N. Kritsky. Pediatriya 36:34-40 (Jan.) 1958 (In Russian) [Moscow].

One hundred four children who had had tuberculous meningitis were under observation at the Children's Tuberculous Sanatorium of the Voronezh Region. Eighteen (9.5%) children had relapses. They were treated with streptomycin (subarachnoidally and intramuscularly) and after 1951 with streptomycin coupled with PAS and phtivazid. Relapses of tuberculous meningitis were more common in children with hematogenic manifestations of tuberculosis, as well as in those with delayed treatment. Most frequently they occurred in the first 12 months from the onset of the disease. These manifestations were provoked by infections, overcooling, trauma, etc. During the last years relapses were fewer in number due to advanced methods of treatment and early diagnosis.

Spontaneous Perforation of Biliary Passages in Infants. R. Funder. Tidsskr. norske lægefor. 78:184-185 (March 1) 1958 (In Norwegian) [Oslo].

Spontaneous perforation of the biliary passages in infants is a rare condition but one it is important to know because immediate surgical treatment is necessary. Some weeks after birth, in an infant previously perfectly well, more or less acute onset of the following symptoms occurs: increasing apathy with crying, vomiting and meteorism, slight jaundice of intermittent type, light stools, dark urine, and slight fever. In the case reported in an infant aged 2 months, laparotomy with injection of indigo carmine via the gallbladder revealed a small perforation in the anterior wall of the hepatic duct at its junction with the cystic duct. A polyethylene tube was placed in the choledochus duct, and the perforation was closed over the tube. The postoperative course was uneventful. Three months after discharge the child was well. The importance of preoperative cholangiography is stressed.

Murmurs in Children: A Clinical and Graphic Study in 500 Children of School Age. A. A. Luisada, O. M. Haring, C. Aravanis and others. Ann. Int. Med. 48:597-615 (March) 1958 [Lancaster, Pa.].

A clinical and graphic study of systolic murmurs was made in 470 unselected children, between the ages of 4 and 14 years, and in 30 adolescents, between the ages of 15 and 17 years. There were 245 boys and 255 girls. Of the 500 children, 350 were white, 146 were Negro, and 4 were Indo-American. Clinical auscultation was made by 3 examiners. Electrocardiograms and phonocardiograms were obtained from all children. Additional clinical and graphic studies were made in 87 children with louder murmurs. Fluoroscopy was done in 40. Hematological studies were made in 38. From a clinical point of view, a medium or loud systolic murmur was detected in 23.3%, and no significant difference was found between the 2 sexes. Even though most of the systolic murmurs were pulmonic, a fair number were heard at the apex and over the aortic area. No correlation was found between murmurs and economic background or race. No correlation was found between murmurs and height or weight. Changes of the murmur with changes of position of the child or by rotating the neck were found to be inconstant and not relevant. No prolongation of the QT interval was found in children with murmurs. A phonocardiographic study revealed diastolic extra sounds in 63% of the children studied and a split pulmonic sound in over 50%. A study of the configuration of the murmur and of the area in which it was best recorded was made. With faint murmurs excluded, 23% of the children had murmurs in the tracing. The murmur was "musical" in more than 50% of the children; it was "diamond-shaped" in slightly less than 50%, and it was "in decrescendo" in more than 50%. This study would seem to indicate a mitral origin in over 50% and a pulmonic or aortic origin in the remainder. In 6.5% of the children, significant differences were found between the results of clinical examination and phonocardiographic findings. Regarding anemia, no difference was found between children with murmurs and those without. Fluoroscopy revealed a dilated and strongly pulsating pulmonary artery in 75% of children with louder murmurs.

The following possibilities were considered and excluded: (1) that the murmur is inherent in the size and configuration of the cardiovascular system of the child; (2) that it is caused by a disproportion in the development of heart, vessels, and ostiums; (3) that it is due to compression of the pulmonary artery by the chest wall; and (4) that it is an extracardiac murmur or is due to anemia or is originating in the neck. It was also excluded that the systolic murmurs of children have different clinical or graphic characteristics from those of "organic" murmurs. The frequency of occurrence of apical and aortic systolic murmurs was not considered as implying a "physiological" origin. Many diseases in man, such as coronary arteriosclerosis, dental caries, or baldness, the incidence of which is extremely common, are not considered physiological. In an attempt to ascertain whether an extremely discrete form of rheumatic fever may provide an explanation for the systolic murmurs of children and adolescents, postmortem examinations were performed on 500 unselected persons over 5 years of age. These studies revealed the extreme frequency with which the cardiac valves present minor damage. This frequency increases with age; lesions were found in 20% between the ages of 11 and 15 years. The coincidence of this figure with that of medium or loud murmurs observed by the authors is striking. These minor valvular lesions were considered by pathologists as being of rheumatic nature. However, further proof of this may be needed. Two alternative concepts are presented: (1) that the murmurs are caused by a discrete rheumatic process which has different characteristics from the more severe forms and which, in most cases, is not followed by important valvular lesions and (2) that the murmurs are due to nonrheumatic, possibly allergic valvulitis, with no tendency to increase in severity. In either case, it is to be considered impossible to separate these murmurs from those of valvular lesions which have greater clinical significance. Therefore, the authors advise careful notation of all murmurs and repeated studies through the years. Mitral stenosis would never be accidentally discovered in patients between the ages of 20 and 40 years if careful, systematic studies of children were made and observations were continued until a murmur either disappeared or became definitely significant.

DERMATOLOGY

Lepromatous Leprosy: Combined Treatment with Sulfone, Streptomycin and Isonicotinic Acid Hydrazide. O. Orsini. Arq. mineir. leprol. 17:291-294 (July) 1957 (In Portuguese) [Belo Horizonte, Brazil].

According to the literature, the administration of sulfones alone in the treatment of persons with leprosy favors the development of pulmonary tuberculosis or aggravates the lesions of pulmonary tuberculosis. A combined treatment with sulfones, streptomycin, dihydrostreptomycin, and isonicotinic acid hydrazide causes a marked regression of both the pulmonary and the leprotic lesions. It often produces complete recovery from both diseases.

A married woman, 40 years old and the mother of 2 children, requested treatment for what she thought were leprotic lesions. The patient had had contact for 6 years with a servant who had lepromatous leprosy. Contact was lost when she learned that the servant had the disease. Ten years later hypochromic spots appeared on the legs of the patient. In the course of 3 years the spots became dark in color. Erythematous lesions appeared on the face. Small nodules appeared on the arms and legs. There was a complete tactile anesthesia of the feet. The results of the Wassermann and Mitsuda reactions were constantly negative. Tests for Mycobacterium leprae in the nasal mucus and in exudates of the nodular lesions became positive after a few years of having been negative. The patient used irregularly for more than 1 year a sulfone preparation in tablets taken by mouth. Then she complained about respiratory symptoms and moderate fever. Roentgenologic examination of the chest showed early lesions of bilateral pulmonary tuberculosis. Treatment consisted of the administration of sulfone in combination with streptomycin, dihydrostreptomycin, and isonicotinic acid hydrazide. Both the pulmonary lesions and the lesions of tuberculoid leprosy greatly and immediately improved. Tests of the nasal mucus and of exudates of the nodular lesions of leprosy became negative for M. leprae. The patient gained weight, her general condition rapidly improved, and she seemed to be on the way to complete recovery.

Inflammatory "Ringworm." R. J. Rowe. Wisconsin M. J. 57:115-117 (March) 1958 [Madison].

The author reviews observations on 58 patients with inflammatory ringworm seen over a period of 6 years at the Marshfield Clinic, in a rural region of Wisconsin, where the condition is rather common. The infection is called "kerion" when it appears on the scalp and "tinea barbae" when it appears in the bearded area; the term "tinea profunda" is sometimes used to describe the disease occurring in other areas of the body. The ages of the patients ranged from 2 months to 62 years. There were 39 males and 19 females. Among the 32 patients less than 14 years of age, there was an equal number of boys and girls, but among those over 14 years, there were only 3 females. The disease is thought to be contracted from animals but not to be infectious from one person to another. Men have more exposure than women as age progresses. The adult scalp resists ringworm infection, but the male beard is very susceptible. Erythema and scaling are the first signs of infection. If the involved areas become edematous, the physician should warn his patient that the "deeper," more inflamed type of ringworm may be present. The infection often progresses to form a nodular, boggy area with many draining sinuses. Even though fluctuation is present, attempts to incise and drain the nodules are often not successful because of the boggy nature of the tissue. Hair in the area tends to break off and may be pulled with ease. Enlarged, tender, regional lymph nodes are usually present. Not infrequently the temperature is elevated, and occasionally a generalized papuloerythematous eruption appears (trichophytid). The disease runs its course in 2 to 4 months but may last longer.

At least in the early stages, the inflammation seems to be primarily an allergic reaction to the tinea. When pustules and drainage occur, secondary bacterial infection may be present. A diagnosis can be established by placing scales of hair from the involved area on a slide, applying a drop of 15% potassium hydroxide solution, then a cover slip, heating to just below the boiling point, and then exerting pressure on the cover slip. If spores or mycelia are present, a positive diagnosis can be made, but the converse is not necessarily true. Particularly in the later stages of the infection it may not be possible to demonstrate spores or mycelia. In the author's series microscopic examination was not performed in all cases, but mycelia or spores were found in 38 of the 58 patients. Cultures were done in 22 of the cases. Trichophyton gypsum was identified in only 4 cases. T. verrucosum frequently causes ringworm in cattle, but the author used Sabouraud's medium, on which T. verrucosum does not grow well. Since fungicidal drugs are largely ineffective, treatment is mostly palliative. During the acute draining stage, hot, wet compresses dipped in Burow's solution should be applied 3 times daily. On the scalp the author uses 1% iodochlorhydroxyquin (Vioform) 3 or 4 times daily. On other areas 1% hexachlorophene in calamine liniment is useful. As the drainage subsides, 2% iodochlorhydroxyquin in yellow petrolatum is applied 3 times daily. This therapy helps to prevent secondary infection.

Molluscum Pseudocarcinomatosum. F. Linell and B. Månsson. Nord. med. 59:226-227 (Feb. 6) 1958 (In Swedish) [Stockholm].

Molluscum pseudocarcinomatosum develops rapidly. In 2 to 6 weeks a cupola-formed skin tumor can develop, as a rule 10 to 20 mm. in diameter, 5 to 10 mm. in height, having in the center a corneous plug. Regression is followed by expulsion of the plug. Healing leaves a more or less conspicuous scar, depending on the degree of secondary infection. There is a great resemblance to squamous epithelial carcinoma. The sites of predilection are the face and hands. The etiology is unknown. The localization to exposed cutaneous areas suggests exogenic influence. In the 10-year period from 1945 to 1954, 533 cases of squamous epithelial carcinoma were registered in the Radiologic Clinic in Lund. On follow-up 99 were diagnosed as molluscum carcinomatosum. The clinical picture was typical of molluscum carcinomatosum in additional cases, but the histological material was insufficient for confirmation of the diagnosis. Abundant biopsy material is necessary to allow a definite diagnosis by comparison of the clinical picture and the histological picture. Two-thirds of the patients with this disorder were men. The average age for both men and women was 59, or about 10 years younger than that for squamous epithelial carcinoma. With purely conservative treatment the cosmetic result is often unsatisfactory. Since 1955 the technique described by Beare and others has been applied in Lund. The tumor is planed off even with the skin surface and the bleeding stilled by thermocautery. Abundant biopsy material for histological examination is thus obtained. If the diagnosis is confirmed histologically, no further measures are taken and excellent cosmetic results have been attained. If squamous epithelial carcinoma cannot be excluded, radiologic treatment is given. The practical consequences of distinguishing molluscum carcinomatosum from squamous epithelial carcinoma are stressed.

Contact Dermatitis from "High-Speed-Duplicator" Papers: A New Disease of Office Workers. C. Sheard Jr., H. J. Spoor and R. Abel. A. M. A. Arch. Dermat. 77:435-437 (April) 1958 [Chicago].

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INDUSTRIAL MEDICINE

Observations on the Course of the Recent Influenza Epidemic and on Its Preventive and Therapeutic Treatment in a Factory Community. C. Rotta. Minerva med. 49:329-337 (Jan. 31) 1958 (In Italian) [Turin, Italy].

The author presents 3 observed phases of an influenza epidemic in a factory community in the fall of 1957: incidence of the epidemic among nonvaccinated children; effect of influenza vaccination in a factory community; and results of preventive and therapeutic treatment of children with influenza by using the serum of convalescents from influenza. Influenza spread among all 1,000 nonvaccinated boys, between the ages of 6 and 12 years, in a children's community center. Most children became ill between the 6th and the 11th day of the epidemic. Mean duration of the disease was from 5 to 6 days. The onset of influenza was sudden and was marked by high fever, headache, malaise, chilliness, and muscular and joint pains. Inflammation of the respiratory tract and gastrointestinal disturbances appeared a few days later. General health remained good, even in the more severe instances. The disease relapsed in 134 children (13.4%). All 200 adults working in the community center also became ill with influenza. The disease did not differ between adults and children either in duration or in symptoms. The considerably higher incidence (4-5 times) of the disease among adults working in the community center, as compared with adults not connected with the center, indicates that during severe epidemics of influenza the length of time exposure to the infectious agent has more weight than individual defensive stamina.

During the same period of the influenza epidemic a study was made on 8,618 factory employees, mostly males, of whom 4,776 were plant workers and 3,842 office employees. They were divided into 2 equal groups, 1 of which received a polyvalent vaccine against influenza and the other constituted the control group. In the vaccinated group, 470 plant workers (19.7%) and 249 office employees (13%) became ill with influenza. In the control group, 551 plant workers (23%) and 487 office employees (25%) became ill. To summarize, 719 of all vaccinated employees (18.7%) and 1,038 of nonvaccinated employees (23%) contracted the disease. There was also a slightly higher incidence of the disease among the plant workers than among the office employees. Vaccination resulted in a lower incidence of the disease and in a lower absenteeism from work.

Serum of convalescents from influenza was administered intramuscularly in doses of 2 to 8 cc. to another group of children as a prophylactic agent. Symptoms were milder and were accompanied by only a slight fever in children who received the serum and became ill as compared with ill children who did not receive the serum. Serum of convalescents from influenza administered to other children with the acute type of the disease brought about a rapid improvement and gradual remission of symptoms. Serum of convalescents from influenza thus has proved to have a certain therapeutic value.

THERAPEUTICS

Spleno-Portal Route in the Treatment of Liver Disease. G. Scevola. Gazz. med. ital. 117:56-62 (Feb.) 1958 (In Italian) [Turin, Italy].

The splenoportal route is presumably an efficacious route for drug administration in the treatment of liver disease because of its anatomic proximity to the liver. The author observed the therapeutic effect of an Italian proprietary preparation of inositol, administered by the splenoportal route to 35 rabbits in which hepatic damage was experimentally produced. Carbon tetrachloride, the toxic substance, was given to all animals in a total dosage of 7.5 cc. per gilogram of body weight for a period of 10 days. Thirty rabbits, which were divided into 3 equal groups, received inositol for 10 days. The first group was given the drug orally in daily doses of 0.50 Gm. per kilogram of body weight. The second group was given the same amount intravenously. The third group was given the drug by the intrasplenic route in daily doses of 0.25 Gm. per kilogram of body weight. The spleen was exteriorized and fixed subcutaneously in order to facilitate repeated injections of inositol into it. Specimens of liver were obtained from the animals by biopsy before and after medication with inositol. A fourth group, consisting of 5 rabbits which were used for control purposes, was given no medication. Liver material was obtained from this group by biopsy at the end of the intoxication and 5 days later.

The rabbits were weighed during the periods of intoxication and medication. They decreased in weight about 200 Gm. per kilogram of body weight during intoxication. They also lost appetite and vivacity. Gradual improvement of these conditions was observed during the period of recovery, and it was more marked in the animals which had received inositol than in those in the control group. Histological examination of liver specimens showed a slightly greater effect of the drug administered by the oral or intravenous route than by the splenoportal route. However, the amount of the drug administered by the splenoportal route was equivalent to half of the amount given by either of the other 2 routes. Two hypotheses may be drawn from the histological findings. One is that the splenoportal route is more efficacious than the oral or intravenous route. The other is that the drug given by the splenoportal route passes unabsorbed through the liver and then returns to it with the arterial blood to be eventually metabolized there.

The Fluid and Electrolyte Therapy of Severe Diabetic Acidosis and Ketosis: A Study of 29 Episodes (26 Patients). H. E. Martin, K. Smith, and M. L. Wilson. Am. J. Med. 24:376-389 (March) 1958 [New York].

The authors report on 16 female and 10 male patients, between the ages of 14 and 73 years, with severe diabetic acidosis and ketosis who were treated at the Los Angeles County Hospital. Three of these patients had 2 attacks of severe diabetic ketoacidosis. Three types of repair fluids of varying tonicity (hypotonic, isotonic, and hypertonic), containing molar sodium lactate, a modified Butler's solution (containing 57 mEq. of plasma electrolytes), and sodium chloride solution, were used with some variation among the patients. Potassium not be possible to demonstrate spores or mycelia. In the author's series microscopic examination was not performed in all cases, but mycelia or spores were found in 38 of the 58 patients. Cultures were done in 22 of the cases. Trichophyton gypsum was identified in only 4 cases. T. verrucosum frequently causes ringworm in cattle, but the author used Sabouraud's medium, on which T. verrucosum does not grow well. Since fungicidal drugs are largely ineffective, treatment is mostly palliative. During the acute draining stage, hot, wet compresses dipped in Burow's solution should be applied 3 times daily. On the scalp the author uses 1% iodochlorhydroxyquin (Vioform) 3 or 4 times daily. On other areas 1% hexachlorophene in calamine liniment is useful. As the drainage subsides, 2% iodochlorhydroxyquin in yellow petrolatum is applied 3 times daily. This therapy helps to prevent secondary infection.

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Aplastic Anemia After Myleran Treatment in Chronic Myeloid Leukemia. J. G. M. Van Esser. Nederl. tijdschr. geneesk. 102:379-381 (Feb. 22) 1958 (In Dutch) [Amsterdam].

The author presents the histories of 2 patients who were treated with busulfan (Myleran) for chronic myeloid leukemia. The first patient had taken 4 mg. of busulfan daily for several months and then 2 mg. daily for 1 month, a total of 364 mg. The second patient had taken 2 mg. daily for 7 months. A hemorrhagic tendency developed in both patients, and aplastic anemia was detected. Repeated transfusions of fresh blood were given to counteract the anemia. These were tolerated at first, but both patients died of cerebral hemorrhage. The author emphasizes that control studies should be made on all elements of the blood at regular intervals during busulfan therapy and for several months after the discontinuation of this therapy.

Treatment of Paralytic Ileus with Cholinesterase Inhibitors in Intravenous Drip. U. Breine, I. Hedenberg, and S. O. Liljedahl. Acta chir. scandinav. 114:172-180 (No. 3) 1958 (In English) [Stockholm].

Fifty patients with paralytic ileus were treated with cholinesterase inhibitors administered by intravenous drip at the Lidköping Hospital in Sweden. Two proprietary preparations of neostigmine in doses of 2 to 4 mg. in 1 liter of dextrose, invert sugar, sodium chloride solution, or a 6% colloidal infusion solution with 0.9% sodium chloride (Macrodex), were given at the usual drip rate of 30 to 35 drops per minute. The patient received the intravenous neostigmine drip for 24 to 48 hours and in exceptional cases for longer periods. A radiographic contrast medium was given a few hours before the drip was instituted in order to make sure that the contrast medium had started to pass from the stomach to the intestine so as to prevent the entire gastric contents being removed from the stomach by vomiting. The patient usually had an indwelling duodenal catheter.

In some patients, intestinal function started after 2 or 3 hours, and in others after about 24 hours; it appeared to be marked in both the large and the small intestine. In only 1 patient who was in poor condition did the neostigmine drip fail to produce any effect. No great discomfort was reported by the patients. No undesirable side-effects were noted except in 1 patient in whom nausea required discontinuation of the drip. No cardiovascular complications occurred. The threshold for intestinal stimulation appears to be appreciably lower than that for cardiac stimulation.

The intravenous administration of cholinesterase inhibitors is indicated chiefly in paralytic ileus and in combinations of this form of ileus with mechanical intestinal obstruction. Cholinesterase inhibitors are contraindicated in the presence of strangulation of the intestine. The stimulating effect of neostigmine on the intestinal activity may be attributed to an increased acetylcholine action on the intestine. In view of the difficulty familiar to the surgeon and the roentgenologist of accomplishing adequate decompression, which is an essential part of the treatment of intestinal obstruction, with an intestinal catheter, the technique of intravenous administration of a cholinesterase inhibitor appears to offer appreciable advantages. Neostigmine drip combined with a contrast meal is also a valuable aid in differentiating between paralytic ileus and partial mechanical obstruction.

Cycloserine-Isoniazid Combination Therapy in Virgin Cases of Pulmonary Tuberculosis. I. G. Epstein, K. G. S. Nair, L. J. Boyd and P. Auspitz. Dis. Chest. 33:371-381 (April) 1958 [Chicago].

Fifty-five men and 26 women, between the ages of 17 and 73 years, with recent pulmonary tuberculosis, who had not been treated previously, were given capsules containing 0.5 Gm. of cycloserine (Seromycin) and 0.3 Gm. of isoniazid daily; the drugs were administered orally in 2 divided doses, morning and evening, for 6 to 16 months. A chest roentgenogram was taken monthly, bacterial examination of the sputum was made bimonthly by smear and culture, and, when negative, examination of the gastric contents was made. Cycloserine plasma levels were obtained at regular intervals. Liver and kidney function tests and peripheral blood studies were also done several times in the course of the therapeutic trial. Sixty-eight (84%) of the 81 patients had some degree of fever, and all the sputums were positive for tubercle bacilli on smear, and confirmed by culture.

Clinical improvement, drop of temperature, lessening of the volume of sputum, and gain in weight occurred promptly in every patient. The administration of a single capsule containing cycloserine and isoniazid was more acceptable to the patients than the usual isoniazid-aminosalicylic acid (PAS) combination. Within 6 weeks, 40% of the chest roentgenograms showed evidence of improvement. The figure rose to 74% in 12 weeks, and it reached 93% for 48 patients treated for 6 months. Evidence of reduction in the bacillary content of the sputum was obtained within 6 weeks of treatment. Within 3 months 80% of the sputums obtained from 64 patients were negative on culture, and at 6 months the figure rose to 87%. Bacillary sensitivity to cycloserine fell slowly and slightly during prolonged treatment with doses of 1 Gm. or more of cycloserine per day. With the daily dose of 0.5 Gm. of cycloserine, there was no evidence of decreased sensitivity. Resistance to isoniazid developed during the administration of the cycloserine-isoniazid compound at about the same rate as was observed when isoniazid was given alone. An untoward reaction occurred in only 1 patient and did not necessitate discontinuation of the treatment. A combination of 0.25 Gm. of cycloserine and 0.15 Gm. of isoniazid given twice daily is to be considered effective and safe therapy against pulmonary tuberculosis in patients previously untreated. The clinical results obtained were superior to those usually obtained from isoniazid-aminosalicylic acid therapy, both in speed and in degree of response, as gauged by changes in the chest roentgenograms and sputum conversion.

Anticoagulant Treatment of Postoperative Venous Complications. M. Alonzo. Riforma med. 72:120-126 (Feb. 1) 1958 (In Italian) [Naples].

One hundred twenty patients with postoperative venous thrombosis or pulmonary embolism were treated with anticoagulants. Varicose phlebitis of the legs and superficial phlebitis of the saphenous vein were present in 15 patients. The disorders were corrected by the use of anticoagulants. Thrombosis of the deep veins of the calf developed in 40 patients and was corrected by prompt administration of heparin. A mild edema, which appeared in most patients, subsided within 3 to 4 days; the patients were able to leave the bed after 4 to 5 days. Thrombosis of the thigh, which developed in 15 patients, required anticoagulant therapy for 15 days. Thrombosis of the iliac vein developed in 5 patients, was more difficult to treat. Complications associated with this disorder were frequent, and there was also a hazard of involvement of the vena cava. Thrombosis of the vena cava developed in 1 patient and required treatment with heparin for 25 days. Venous thrombosis associated with arteriospasm developed in 2 patients. This disorder was effectively treated by a combination of procaine hydrochloride and heparin. Phlebitis of the arm, which developed in some patients, was easily managed. Embolism of the pulmonary artery, which affected other patients in this series, required prolonged anticoagulant therapy. Procaine hydrochloride, papaverine, cardiac tonics, and oxygen were added to heparin for the treatment of this complication.

Dark skin pigmentation and permanent edema were the most common sequelae observed. They were due to too late institution or too early withdrawal of anticoagulant therapy. Hemorrhage occurred in only 1 patient. It developed in a woman, 20 years old, who before admission to the hospital had taken 20 tablets of Dicumarol on the erroneous impression of taking a tonic treatment. Hemorrhage was corrected with considerable difficulty. The author believes that anticoagulant therapy is the most important aid in controlling postoperative venous complications. Selection of the right dosage is essential because of the narrow margin between the therapeutic dosage and one producing hemorrhage.

PATHOLOGY

Abnormal Entering of All Pulmonary Veins into the Left Innominate Vein, with Interatrial Communication (Taussig-Snellen-Albers Syndrome). I. Ferrario. Schweiz. med. Wchnschr. 88:256-261 (March 15) 1958 (In German) [Basel, Switzerland].

The author reports on a 4½-year-old girl and a 10-day-old boy with abnormal entering of all pulmonary veins into the left innominate vein, combined with an interatrial septal defect but without any other major cardiac malformation. The term "Taussig-Snellen-Albers syndrome" is suggested for this malformation of the pulmonary veins. The chest roentgenogram of the girl showed the typical figure-8 shape, formed by the widened shadow of the upper mediastinum and the enlarged cardiac shadow. The death of this patient resulted from acute pulmonary edema, since failure of the right ventricle had its repercussions in the lesser circulation. Autopsy was performed and revealed a common vertical ascending venous trunk on the left side, through which the pulmonary veins entered the innominate vein. The boy died in a hypoxemic state caused by pronounced pulmonary congestion due to stenosis of a common ascending pulmonary artery on the left side, through which the pulmonary veins entered the innominate vein, as revealed by autopsy. Of 22 patients with congenital malformations of the heart and the large vessels, who died in the course of the first 6 months of 1957 and on whom autopsies were performed at the pathological institute of the University of Zürich, only these 2 patients had the Taussig-Snellen-Albers syndrome. Fifty-seven similar cases were collected from the literature, in 35 of which the diagnosis was established at autopsy and in 6 at surgical intervention; in 16 cases a clinical diagnosis was made with the aid of cardiac catheterization and angiocardiography.

Pathogenetically, this malformation is due to an arrest of growth of the sinoatrial region at the end of the first month of embryonic life, either with lack of formation or with secondary closure of a connection between the pulmonary venous system and the heart. As a consequence, persistent anastomosis between the plexus pulmonalis and a remainder of the left vena cardinalis cranialis (left vena cava superior) occurs from which the truncus venosus communis develops. There is hypoplasia of the left atrium, hypotrophy of the left ventricle, and hypertrophy of the right ventricle resulting from the extra load placed on the heart. Occasionally, the additional load placed on the pulmonary circulation may cause thickening of the media of the small pulmonary arteries. In the reported case of the girl, a congenital pericardial diverticulum of the posterior wall was detected, an interesting embryologic condition. The clinical diagnosis of this syndrome may be presumed by the figure-8-shaped chest roentgenogram. Other symptoms observed are dyspnea on exertion, cyanosis, pulmonary congestion, with frequent bronchopneumonia and progressive heart failure. Electrocardiograms show hypertrophy of the right ventricle, .sometimes also hypoplasia of the left ventricle. The diagnosis must be confirmed by angiocardiography and catheterization of the heart. The prognosis depends on the possibilities of compensation of the right ventricle. According to the cases collected from the literature attempts at surgical intervention in this type of malformation have failed.

Histological and Histochemical Changes of Rat's Sarcoma in the Process of Its Cure by Sarcolysin and Dopan. L. F. Larionov and M. A. Presnov. Arkh. pat. 20:32-39 (No. 1) 1958 (In Russian) [Moscow].

Transplantable spindle-cell sarcoma (sarcoma 45) of rats was completely cured by new antitumor preparations—Sarcolysin [dl-p-di (2-chlorethyl) aminophenylalanin] and Dopan [2.6-dioxy-4-methyl-5-di (2-chlorethyl) aminopirimidin]. Pronounced changes were observed in the effect of Sarcolysin on the parenchyma as well as on the stroma of the tumor. The first signs of injury to the tumor were decrease of mitotic activity and disintegration of the nuclei of certain cells with formation of lumps. Later the size of the remaining cells considerably increased, their nuclei and nucleoli became larger, cells with numerous nuclei appeared, the fat was revealed in the cytoplasm, while the ribonucleic acid disappeared.

The injured cells were subjected to lysis. The process of healing included development of a large number of collagen fibers with disappearance of argentophilic fibers. The alkaline phosphatase activity increased during the process of treatment, first in the injured cells and later in connective tissue stroma of the tumor. The change in the parenchyma, i. e., of the tumor cells, is probably the primary factor in the process of cure, while the stroma reaction is secondary. However, the latter promotes the healing. Disturbance of nucleoprotein metabolism, especially in the nucleus, plays an important role in the mechanism of the therapeutic action of Sarcolysin and Dopan on the tumor.

Primary Hyperparathyroidism (Recklinghausen's Osteitis Fibrosa Cystica). J. Lauweryns. Belg. tijdschr. geneesk. 14:1-16 (Jan. 1) 1958 (In Flemish) [Leuven, Belgium].

The clinical picture of hyperparathyroidism varies. When the patient is first seen, the physician may think of osteomalacia, osteomyelitis, skeletal carcinomatosis, chronic arthritis (senile, postmenopausal), secondary hyperparathyroidism with renal osteodystrophy, nephrolithiasis, Paget's disease, multiple myeloma, or polyostotic fibrous dysplasia. The histopathological picture of hyperplasia and of adenoma of the parathyroids is described, particularly with regard to differential diagnosis. The author prefers the term "metastasizing adenoma of the parathyroid" over "parathyroid carcinoma." The symptomatology is discussed with regard to the skeletal, hematological, urinary, gastrointestinal, and vascular systems. The histories of 3 patients with primary hyperparathyroidism are presented. The first patient had pure hyperplasia without the classical symptoms of osteitis fibrosa cystica generalisata but with scleroderma. The second and third patients had trabecular and medullary adenoma, respectively, with the clinical aspects of Recklinghausen's osteitis fibrosa cystica.

RADIOLOGY

Bronchiolar-Cell Carcinoma. J. H. Woodruff Jr., R. E. Ottoman and F. Isaac. Radiology 70:335-348 (March) 1958 [Syracuse, N. Y.].

Bronchiolar carcinoma is different from bronchogenic carcinoma. The authors report 16 cases to illustrate the various features of the condition and cite observations by other investigators. The most common synonyms for bronchiolar carcinoma are alveolar-cell carcinoma, pulmonary adenomatosis, papillary adenocarcinoma, and mucous carcinoma; others are primary multiple carcinoma, multicentric papillary adenocarcinoma of the lungs, columnar-cell carcinoma, alveolar-cell tumor, malignant adenomatosis, and multiple nodular carcinoma. Bronchiolar carcinoma is a primary lung tumor probably originating in the terminal bronchioles in the peripheral portions of the lung. It is composed of tall columnar or cuboidal mucus-secreting cells lying on an intact alveolar septum. It does not, as a rule, destroy the normal pulmonary tissue. The authors are making no distinction between this tumor and pulmonary adenomatosis. The distinctive histological pattern and pathogenesis set this tumor apart from other pulmonary neoplasms. These tumors are usually found in the peripheral portion of the lung; rarely major bronchi may be invaded late. There are no favorite sites. The tumors may be multiple or solitary, varying in size from those measuring a few millimeters in diameter to tumors involving the whole lung. A large mass may be present in 1 section, and multiple small nodules may be found in another section or sections. Metastatic spread by extension to contiguous areas, by the lymphatics and by the blood stream, are well established.

The ages of the 16 patients presented by the authors ranged from 33 to 83 years. A tabulation, in which the various aspects of bronchogenic and bronchiolar carcinoma are compared, shows that the sex incidence of bronchiolar carcinoma is about equal, whereas bronchogenic carcinoma predominates in males. In summarizing the radiologic features of bronchiolar carcinoma, the authors emphasize among other factors that the shadows vary considerably in size. At first they are small and faint, but they tend to grow persistently and progressively. As this occurs, their density increases. The initial roentgenologic finding may be a solitary nodule or infiltrate, a localized cluster of small densities, or diffusely scattered shadows throughout the lung. The shadows tend to combine to form larger "coin," pneumonic, or mass lesions. The margins of the shadows vary from fairly sharp to very indistinct. Dissemination to the same or the contralateral lung is common. In some patients lesions are disseminated on the first examination. Pleural effusions may obscure the primary lung tumor. They may occur on the homolateral or the contralateral side. The shadows may appear to clear at times as their pneumonic or focal atelectatic components resolve. The character of the primary and secondary lesions is not necessarily the same, as one may be nodular and the other infiltrative. While mediastinal adenopathy is discovered on pathological examination in 25% of the patients, it is not common in radiographic studies. Early localized lesions are best treated by resection of the lesion. Radiation therapy has been tried, but, in general, results have been discouraging. The need for early radiologic diagnosis is emphasized. Persistent nonregressing shadows and all mass lesions deserve study by cytological examination, bronchoscopy, bronchography, biopsy possibly by aspiration, and exploratory thoracotomy.

Erosive Rib Lesions in Paralytic Poliomyelitis. C. Bernstein, W. D. Loeser and L. E. Manning. Radiology 70:368-372 (March) 1958 [Syracuse, N. Y.].

The authors call attention to erosive rib lesions which they observed in chest films of 14 of 28 patients with paralytic poliomyelitis, who were being studied at a respirator center. These rib changes did not occur earlier than 10 months after the onset of paralysis, were most frequently seen after 20 months, and in 1 instance did not appear for 45 months. The 3rd rib was involved most frequently, but the 2nd, 5th, 7th, and 8th ribs also showed similar lesions. Localized shallow indentation and narrowing of the upper rib margin were initially noted, progressing without regeneration or other signs of healing to almost total disappearance of bone structure. The rib lesions were unrelated to the age or sex of the patient, to type of therapy, or to presence of decubitus ulcer. No clinical signs or symptoms were attributable to the rib involvement. The most severely paralyzed patients showed the greatest frequency of rib involvement. In view of the localization of the rib erosion, continued pressure of the medial margin of the scapula against the posterior aspect of the rib appears to be the causative factor, although the reason for some patients being spared is not yet determined.

A New and Simple Approach to Air-Contrast Studies of the Stomach and Duodenum. K. Amplatz. Radiology 70:392-394 (March) 1958 [Syracuse, N. Y.].

Various methods have been tried to produce double-contrast studies of the stomach and duodenum, such as the use of effervescent powders and carbonated beverages, the conscious swallowing of air, the insufflation and inflation of the stomach by means of inserted tubes, and the utilization of the air physiologically present in the stomach. The author presents the "straw technique" as a simple approach to air-contrast studies. Only an ordinary drinking straw, either paper or plastic, which has been punctured midway to produce a small perforation, is necessary. By means of this device one obtains simultaneous aspiration of barium mixture and air when the opaque medium is sipped. The size of the perforation in the straw is an important factor. The hole should be very small to allow the formation of only tiny air bubbles within the contrast material. This will insure an easily swallowed bolus containing both air and barium. A larger perforation requires excessive effort on the part of the patient, and the end-results are less favorable, as a smaller amount of air actually is swallowed. A through-and-through perforation of the straw made with a very small sewing needle proved most suitable.

Usually sufficient air will have entered the stomach when the patient, in the upright position, has ingested 2 to 3 oz. of the medium. Certain conditions must be met in order to obtain good contrast films. With carbonated drinks or effervescent powders, the amount of gas liberated is not easily controlled, and frequently overdistention, with consequent obliteration of mucosal detail, occurs. The patient may inadvertently respond to such overdistention by eructation, resulting in complete loss of gas. With the "straw technique" only a moderate amount of gas is introduced into the stomach under fluoroscopic control. One need not be concerned about perforating an ulcer by excessive distention of the stomach. There is no dilution of the opaque medium. One of the chief advantages is that disturbing gas bubbles, which serve to distort the mucosal detail, are held to a minimum. In the past 3 years the author has found this simple and inexpensive procedure to be a most satisfactory approach to double-contrast studies of the upper gastrointestinal tract.

Pneumopericardium Following Sternal Bone Marrow Aspiration: A Case Report. J. L. Ackerman and J. W. Alden. Radiology 70:408-409 (March) 1958 [Syracuse, N. Y.].

An 18-year-old woman with fever of undetermined origin was subjected within a week to 2 chest roentgenograms, neither of which revealed any abnormality. During a bone marrow aspiration of the sternum, which was performed 10 days later, the physician thought he had gone too deeply, but the patient exhibited no reaction. The attempt to aspirate marrow was unsuccessful, and the procedure was postponed until a later date. Another roentgenologic examination of the chest on the day after the attempted sternal aspiration disclosed pneumopericardium. Four days later air was still demonstrable along the left cardiac border. Eventually it disappeared completely.

ANESTHESIA

Hypothermia in the Treatment of Cerebral Tumours. C. B. Sedzimir and J. W. Dundee. J. Neurosurg. 15:199-206 (March) 1958 [Springfield, Ill.]

This report is concerned with the use of hypothermia at the Neurosurgical Center in Liverpool, England. The aim was not simply to use hypothermia but to combine it with controlled hypotension (produced by ganglion blocking drugs) when required. Chlorpromazine, with or without meperidine and/or Phenergan, is used for preoperative medication. Light general anesthesia is induced with thiopental, the larynx is sprayed with 4% lidocaine, and oral intubation is carried out with a flexometallic tube. A large flow of nitrous oxide-oxygen (with a T-piece open-circuit apparatus) and ether is used for the first 10 to 20 minutes to aid the peripheral vasodilatation. Surface cooling is commenced, once the patient is asleep, by application of ice bags all over the body and by laying the patient on a large ice pack. The position of the ice bags is changed frequently, and the patient is tipped in the head-down position at regular intervals to promote redistribution of the cooled blood. The ice is removed at 33 to 31 C (91.4 to 87.8 F), depending on the build of the patient and the final temperature required. The after-drop usually varies from 1.5 to 3 C. Unless the temperature has fallen below 28 C (82.4 F), no attempts at rewarming are made at the end of the operation. When necessary, radiant heat is applied until this temperature is reached. In the absence of any active means of rewarming, the normal body temperature is usually reached within 12 hours of the end of the operation.

During the first few months hypothermia in the Liverpool unit was reserved exclusively for operations on patients with vascular lesions and highly vascular tumors, such as meningiomas and acoustic neuromas. With the passage of time it was induced in patients with practically any type of tumor above or below the tentorium in the presence of considerable or long-standing raised intracranial pressure. Of a total of 174 operations under hypothermia, 94 were for cerebral neoplasms. The operating time was shortened by about one-third. The ease with which it was possible to operate with greater precision and with minimal operative trauma to the brain and blood vessels was of even greater importance. This reduction in operative trauma and in the necessity for occluding cortical veins is regarded as the main reason for the low incidence of cerebral edema. Another advantage of operating under hypothermia has been the fall in the intracranial pressure with reduction of brain volume. Even in the presence of large neoplasms, advanced papilledema, and dulling of consciousness from increased intracranial pressure, the exposed dura mater was not tense. The brain did not bulge, it was frequently shrunken and dry, and the dissection of tumors did not necessitate the same amount of manipulation and retraction. No death was caused by hypothermia. Although the number of tumors operated on with the help of hypothermia is still small, the authors believe that in neurosurgery a moderate cooling to 28 to 30 C (82.4 to 86 F) is entirely safe and that this degree of cooling offers all the advantages of the method.

PHYSIOLOGY

Altered Circulation in the Bone After Distal Diaphysial Fractures of the Tibia: Experimental Studies. G. Fonda and L. Giordano. *Minerva ortop.* 8:589-592 (Dec.) 1957 (In Italian) [Turin, Italy].

Clinical experience has shown that it takes a longer time for consolidation of a bone fracture at the medial or lower third of the tibia than at other sites of the body. Some workers believe that this phenomenon is due to interruption of the nutrient artery, which is supposedly the sole blood conveyor to the medial or lower third of the tibia. The authors observed the reproductive process of vascularization in an artificially produced fracture at the lower third of the tibia in guinea pigs and arrived at a different conclusion. The bone fracture did not greatly alter the blood supply to the bone cortex and to the periosteum. Interruption of the nutrient artery did not discontinue the regular blood flow to the inner layers of the bony stumps. Blood flow could have been maintained only through a great number of anastomoses in the bony stumps, which are confluents to the network of the periosteum. It is more difficult to interpret the blood flow through the medullary vascular network. In view of the interruption of the nutrient artery, continuity between the medullary and epiphysial networks and the vessels of the bone cortex can be assumed. The authors believe that probably a similar reproductive process of vascularization in a fracture at the lower third of the tibia takes place in human beings.

Circulatory Physiopathology of Fractures: I. Vascular Alterations of Fractures of the Upper Limb. G. Fonda and L. Giordano. Minerva ortop. 8:593-595 (Dec.) 1957 (In Italian) [Turin, Italy].

The authors performed experiments on guinea pigs by producing artificial fractures at the medial third of the humerus and of the forearm. A vasodilating process occurred near the fracture site promptly after the induced fracture of the humerus. This process was evident in a lesser degree after the induced fracture of the forearm. No qualitative or quantitative alteration of circulation was seen in the bone or in the surrounding soft tissue. A varying degree in intensity of hyperemia, which appeared in the internal networks of the bone, was consistent with the relative abundance or scarcity of the normal physiological pattern of vascularization. Vasodilative reactions were followed by vascular regeneration. The new blood vessels ran a twisted and irregular course, which turned gradually parallel to the bone axis. The formative process of vascularization penetrated into the bone callus from the surrounding connective tissue and from the stumps. Vascularization of the stumps consisted mainly in the proliferation of the medullary network, whereas contribution of the diaphysial vessels was small. The new network in the periosteum tended to localize on the surface of the bone callus. The interosseous artery became the origin of a rich vascular network after the fracture of the forearm occurred. A parallelism between the development of the vascular pattern and the formation of the respective bone callus could not be traced. Fractures of the forearm caused a quicker and more marked appearance of hyperemia, as well as a richer reproduced vascular pattern, than other fractures. Consolidation of fractures of the forearm was also slower than that of other fractures. The opinion of the authors is that hyperemia and vascular regeneration are related to proliferation of the connective tissue rather than to formation of bone callus.

Circulatory Physiopathology of Fractures: II. Vascular Alterations of Fractures of the Lower Limb. G. Fonda and L. Giordano. Minerva ortop. 8:596-598 (Dec.) 1957 (In Italian) [Turin, Italy].

The authors made analogous experiments on guinea pigs, as reported in the preceding article. Artificial fractures were produced at the medial third of the femur and of the tibia. Vascular alterations in the thigh and in the leg consisted in an active hyperemia and in vascular regeneration. These changes occurred in the adjacent soft tissue, in the bone medulla, in the periosteum, and to a less extent in the diaphysial cortex. These processes were more intensive and took a longer time in the femur than in the tibia. Thirty days after the induced fracture the reproductive process of vascularization in the femur was fully developing, whereas in the tibia it reached the stage of stabilization.

Better conditions for vascular redevelopment were observed in the femur than in the tibia. During the process of vascular regeneration no avascular areas were noted in the region of the femur fracture, but they were noted in the case of tibia or upper limb fracture. This observation has indicated that the period of fracture healing is not directly related to the process of regional vascularization. Although conditions of vascular regeneration are better in the case of fractures in the thigh than in the arm, yet consolidation of a diaphysial fracture of the femur takes more time than consolidation of a humerus fracture. Consequently, it is not possible to establish a relationship between the time of the fracture consolidation and alterations in the regional circulation after the fracture. The interosseous artery participated in the vascularization process of the bone callus which followed fracture of the forearm. A homologous process was not evident in the vascularization process which followed fracture of the leg.

BOOK REVIEWS

The Neuroses and Their Treatment. Edited by Edward Podolsky, M.D., F.A.P.A., F.A.P.M. Cloth. $10. Pp. 555. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1957.

There is so much difference of opinion among psychiatrists and so many facets to the total field of psychiatry that it is impossible to write a definitive textbook. For this reason, several monographs, such as this one, covering one aspect of the subject have been published. The editor has selected 40 contributors who have written about special phases of the neuroses. Although there may be some differences of opinion as to the wisdom of including some of these papers, the editor has chosen wisely for the most part. The papers deal with problems in childhood, various syndromes, and methods of treatment. Some of the authors have written in too great detail and with terminology which may be difficult for the general practitioner or the medical student. The book does not have an index, nor is there a bibliography for any one of the chapters. It is, however, authoritative for the fields it covers and is recommended for use by persons interested in the neuroses and their treatment.

Surgical Forum. Volume VIII; Proceedings of the Forum Sessions, Forty-third Clinical Congress of the American College of Surgeons, Atlantic City, New Jersey, October, 1957. Cloth. $10. Pp. 671, with illustrations. American College of Surgeons, 40 E. Erie St., Chicago, 1958.

This book is a continuation of the publication of brief communications presented in the sections referred to as the "Surgical Forum" that are now an established part of the Annual Clinical Congress of the American College of Surgeons. Most of the papers are excellent. They are brief and easily readable, and the discussions are all to the point. Pertinent bibliographies are included at the end of each presentation. The reports deal with shock; fluids, electrolytes, and parenteral nutrition; wound healing and infections; trauma, burns, and radiation injury; cancer; liver and biliary tract; pancreatitis; heart; pulmonary physiology, anesthesia, and thyroid gland; gynecology and obstetrics; neurological surgery; orthopedics; plastic surgery; and urology. Most of the reports are by younger men who are in training or have recently completed training, with older men as collaborators. Clinical experimental observations and animal experiments are often dealt with in the same report, and results of work in both clinical and laboratory aspects of the problems are presented in each of the major sections. The great significance of this volume, as of the previously published volumes, lies in the fact that an excellent summary of what is going on in experimental surgery and clinical investigation is made available. Moreover, in these forums, which are being received with increasing enthusiasm, the younger generation of surgeons is given an opportunity to be heard at a national level by a large and sympathetic audience. Not the least important aspect in this situation is the fact that by means of these forums these younger workers do not have to wait for long periods to be heard in person by large numbers of their colleagues from all over the country and by those older than themselves. The American College of Surgeons deserves great credit for affording these opportunities to the younger men.

Traquair's Clinical Perimetry. By G. I. Scott, M.A., M.B., F.R.C.S., Professor of Ophthalmology, University of Edinburgh, Edinburgh, Scotland. With foreword by Norman M. Dott, C.B.E., M.B., F.R.C.S., Professor of Neuro-Surgery, University of Edinburgh. Seventh edition. Cloth. $17. Pp. 333, with 280 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Henry Kimpton (medical book department of Hirschfeld Brothers, Ltd.), 134 Great Portland St., London, W. 1, England, 1957.

When Traquair published the first edition of his "Introduction to Clinical Perimetry" in 1927, it quickly became the standard textbook on this subject in the English speaking world, being widely adopted by ophthalmologists, neurologists, and neurosurgeons. His concept of the visual field as "an island of vision in a sea of blindness," his graphic descriptions of the topography of that island, his promotion of the values of quantitative perimetry, and the lucid interpretation of perimetric and tangent screen findings served to make his book a classic in the field. Each subsequent edition showed further improvements, the sixth edition having appeared in 1949. Dr. Traquair died in 1954 at the age of 79. The present author has retained much of the original flavor of the previous editions but has brought the work up to date. He has emphasized the value of the confrontation test, rewritten the chapters on glaucoma and affections of the optic nerve and chiasm, and added some new illustrations. Some of the newer developments, such as flicker fusion fields, the use of luminous test objects by "dark light" perimetry, and the multiple-pattern method for quick screening, either are not mentioned or are briefly dismissed. Not as complete in this regard as Harrington's "The Visual Fields," issued by the same publisher, this new edition of Traquair's monumental treatise nevertheless deserves a prominent position in the library of every physician concerned with perimetry as a diagnostic and prognostic aid.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

PERSISTENT PYURIA FOLLOWING PROSTATECTOMY

To the Editor:—*A 75-year-old man has had pyuria (4+) ever since he underwent a transurethral prostatectomy a year ago. He has had only one febrile reaction since his operation. A stained smear of urine sediment revealed what appeared to be a gram-negative diplococcus, intracellular, resembling Neisseria gonorrhoeae very much. A pure culture of tribe Mimeae was reported. Bacterial sensitivity tests revealed that the organism was somewhat sensitive to antibiotics. Is there any drug that would have a specific effect on this organism and would be likely to eradicate it from the urinary tract?*

Hinton J. Merritt, M.D., Colquitt, Ga.

Answer.—The species Mimeae is, in essence, a gram-negative bacillus, but, because of bipolar staining, it may resemble a gram-negative diplococcus. There is no report that this organism is naturally sensitive to the antimicrobial agents, so it it likely that such resistance has been acquired. It is not uncommon after transurethral resection of the prostate for pyuria to persist indefinitely, and the urine can be cleared of pus only temporarily. Since this patient has had only one febrile reaction, the best management would be to forego any intensive therapy and to institute treatment only when he has some subjective symptoms, such as fever or dysuria. It is likely that one of the sulfonamides—even though the Mimeae are resistant in vitro—would control such symptoms, because of the higher concentration in the urine than in the serum.

ELECTRICAL CONDUCTIVITY OF BLOOD

To the Editor:—*Please give information relative to the conductivity and/or specific resistance of human blood.*

F. J. Kelly, M.D., Amarillo, Texas.

Answer.—The ability of a solution to conduct an electric current depends on the number of ions available in solution and on the velocities with which these ions move in the electric field. The specific resistance of a conductor is the resistance in ohms offered by a cube of the substance or solution 1 cm. long by 1 sq. cm. *in cross section.* The specific conductance is the reciprocal of the specific resistance and is expressed in reciprocal ohms or mhos. The specific conductance of human serum at 18 C is about 110×10^{-4} reciprocal ohms. The conductance of serum is a function of the number (per unit volume) and mobilities of all the ions present. There are additional factors which influence the conductance of serum. These are the total protein level, the pH of the serum, and the temperature. The relation between specific conductance and the "total base" of serums of varying protein content at a given temperature has been studied by Sunderman, who has derived a formula and chart relating these factors (*J. Biol. Chem.* **143**:185, 1942; *Am. J. Clin. Path.* **15**:219, 1945).

TIGHTNESS IN THE CHEST

To the Editor:—*A 35-year-old woman has been having "spells" which started about 14 months ago. Her symptoms at that time were "strange feeling and tightness" in her chest. These have become progressively worse, and new symptoms have appeared. The first addition was pain in her chest and, later, in both arms. The last episode, which was witnessed, occurred a few days ago, when she complained of feeling the pain in her chest and down her arms. Objectively, her superficial leg and arm veins were very much dilated. She said she also felt weak and faint. Her hands were dark red, almost cyanotic in appearance, and her feet were similarly discolored. These episodes have lasted from about 15 minutes to several hours. She is well between attacks. She had the book thrown at her in the laboratory and it came out second best—all findings in the tests were normal. The x-ray department reported a congenital heart defect, a patent foramen ovale. Her blood pressure is usually 100/75 mm. Hg; however, it has ranged down to 80/50 at times. She has been to several doctors and hospitals and no one can explain these bizarre symptoms. Please supply diagnostic assistance.*

M.D., Michigan.

Answer.—The sensations of pressure in the chest and the pains radiating down the arms seem to indicate that there is some cardiac disease. The clinical picture conforms with the description that one finds with coronary insufficiency. It is assumed that electrocardiograms did not show any abnormalities of the conductive system and that there are no abnormal findings in the lungs. However, the x-ray department did report a patent foramen ovale. The prominence and dilatation of the veins in the upper and lower extremities suggest some

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

embarrassment on the venous return involving the superior and inferior vena cava. Since this occurs at the same time, it may be assumed that the causative factor is where the cava are close together, which would signify the right auricle. The dilatation of the veins is probably not due to any involvement or disorder of the peripheral venous system. This would seem to be connected with some clinical disturbance of the normal cardiac function. It is difficult to decide whether it is due to a ball-valve embolus or possibly some tumor in the heart or other abnormality which is disturbing the normal cardiac function. The solution of the problem could be more definitely crystalized if this case were studied with the newer techniques in cardiology, namely, angiocardiography, catheterization of the heart, and an estimation of the oxygen content in the chambers. Investigation of the patent foramen ovale may throw further light on the problems. Management will depend on the results of the findings.

MEPHENESIN FOR MUSCLE PAINS

To the Editor:—*A 54-year-old woman feels fine all day, but as soon as she falls asleep she is suddenly awakened with pains (not cramps) in many parts of the skeletal area. She has been troubled this way for years. She is not neurotic. In order to relieve her distress, she arises and walks about, and she is immediately relieved. Since mephenesin preparations give more relief than anything else that has been tried, please give further information on this type of therapy.*

Horace A. Hall, M.D., Corona del Mar, Calif.

Answer.—Mephenesin (in the United States) or myanesin (in Great Britain) is an aromatic glycerol ether (3-*o*-toloxy-1,2-propanediol). Berger and Bradley (*Brit. J. Pharmacol.* 1:265, 1946) thought that, due to the depressant action of mephenesin on certain polysynaptic pathways in the spinal cord, skeletal muscular relaxation took place without loss of consciousness. Their work stimulated various investigators to study the diminution of skeletal muscular tone and involuntary movement in such conditions as muscle spasm of traumatic origin, rheumatic arthritis, tetanus, and various neurological hyperkinetic states. Reports of ineffectiveness of this drug have appeared, but there is evidence that it has been of some value in patients with hypertonus of skeletal muscle and spasticity. Domino, who has published the most recent comprehensive work on mephenesin and mephenesin-like substances, stated that mephenesin may be strikingly effective in some cases of spasticity and completely ineffective in others (*Ann. New York Acad. Sc.* 64:705, 1956). Thus, the transient duration of action of mephenesin and low order of potency when given orally do not produce uniformly effective results.

VASOSPASM OF THE RETINAL ARTERIES

To the Editor:—*A patient, 60 years of age, had a thrombosis of a branch of the left retinal artery 10 years ago and a thrombosis of branches of the right retinal artery 1 year ago and again one month ago. There has been no other evidence of vascular disease. The blood pressure, electrocardiogram, serum cholesterol level, and sedimentation rate are all within normal limits. Funduscopic examination of the uninvolved vessels revealed normality compatible with the patient's age. After the second thrombosis, therapy with bishydroxycoumarin was instituted; however, the prothrombin time was below therapeutic levels at the time of the last thrombosis. Could vasospasm be a primary or contributing factor in these multiple thromboses? If so, would papaverine hydrochloride, tolazoline hydrochloride, and/or other vasodilator drugs be of value? Please give further suggestions for therapy.* *M.D., New York.*

Answer.—Vasospasm, if not a contributing factor to thrombosis of retinal arterioles, is certainly an accompanying one. It is now felt that emboli almost never occur in the retinal arterial tree and that even primary thromboses are rarer than was formerly believed. Therefore, vasodilators are definitely indicated for the acute retinal arterial (or arteriolar) occlusion and are best administered by retrobulbar injection. However, the benefits to be derived from a vasodilator as a prophylactic agent are less clear cut. It is most difficult to keep retinal or choroidal vessels dilated. Carbon dioxide inhalation will cause dilatation of choroidal vessels and increased blood flow, but this has not been demonstrated for the more commonly used vasodilators. Nevertheless, it would be wise to use such a drug as nicotinic acid or beta-pyridyl-carbinol tartrate in the management of this patient. The suggested dosage is 50 mg. three times a day.

HEREDITARY TRANSMISSION OF RETINOBLASTOMA

To the Editor:—*A 16-year-old girl had her right eye enucleated at the age of 2 years for a retinoblastoma. The removal of the eye was followed up with x-ray treatments. She has been apparently well since then. At the present time, she is wondering what chances her future children will have of inheriting her eye condition. Genetically speaking, how can one answer her question?*

Abe L. Feuer, M.D., Gastonia, N. C.

Answer.—A great deal of attention has been devoted to this question recently. The data show that only 25% of patients with such sporadic cases transmit the disease to some of their offspring. The reason that 75% of the patients do not have affected offspring is that in some cases the mutation is in the somatic cells only, in some the family size was too small to permit affected offspring from appearing due to chance factors, or, perhaps, in some a nongenetic accident occurred. If the girl is a transmitter, less than 50% of her children could be expected to have retinoblastoma, since the dominant gene is not always expressed. It is thought that the expectation is about 40% that each child would develop the trait instead of the 50% expectation when the trait is always expressed if the gene for it is present. Tucker and others give a more complete explanation (*A. M. A. Arch. Ophth.* 57:532, 1957).

IPRONIAZID FOR ANGINA PECTORIS

To the Editor:—*The question and answer concerning heart disease and hemoptysis in* The Journal, *March 15, 1958, page 1401, prompted this question on the use of iproniazid in the following case. The patient, 78 years of age, is asymptomatic except for nerve precordial sensations (no real pain) on effort. He is slightly underweight but has never been hypertensive. Findings in the usual laboratory examinations are normal. The electrocardiogram reveals some heart block, and slight enlargement is shown on x-ray. His pulse rate is usually in the low 60's. The history is noncontributory. Would it be advisable to use iproniazid in this case? How and when should it be given, and in what dosage?*

Louis Shalet, M.D., Jamaica, N. Y.

Answer.—Iproniazid should be given only under supervision and by persons who have experience with the drug. It has recently been used in treatment of angina pectoris; reports were first published by Cossio (Buenos Aires) and Cesarman (Mexico City) a year ago and last October respectively. Iproniazid is an unusual drug, very helpful in angina pectoris, but it has to be used with caution because of toxic side-reactions. There will be papers published on this subject, and it is not advisable to use the drug at present, particularly in a 78-year-old man.

TOXICITY OF "TALC"

To the Editor:—*Could soapstone particles ("talc"), if inhaled over a prolonged period of time, produce fibrosis of the lungs?*

Burt Friedman, M.D., Memphis, Tenn.

Answer.—There are many different forms of talc (soapstone or steatite), which basically is a hydrous magnesium silicate. This compound per se is not fibrogenic, but most commercial preparations of talc contain varying amounts of tremolite, which is a fibrous magnesium silicate. Lung fibrosis resembling asbestosis can result from heavy and prolonged exposures to such fibrous compounds, including typical asbestos bodies in the microscopic sections. Also, some talc preparations may have quartz impurities, which might result in a lung fibrosis resembling silicosis after heavy and prolonged exposures. Specimens of the talc under suspicion ought to be given careful minerological studies before too definite conclusions are drawn.

"WHITE VISION"

To the Editor:—*A 45-year-old man has had both eyes removed and now complains of "white vision" present almost continuously while he is awake. He notes that emotional upsets make it worse. His history is somewhat vague. His mother is said to have had rubella before he was born. One eye was removed at the age of 6 months because of a tumor of some sort. He apparently had a congenital cataract on both eyes. In 1935, the cataract was removed and his vision was improved but was still far from normal (he states 40% of normal). In 1942, this remaining eye was removed for intractable pain (glaucoma) and the white vision sensation. He has never been free of this sensation except for a few days at a time since then. Is there any therapy for this condition? Is there any known cause?*

M.D., Ohio.

Answer.—"White vision" is not rare in adults who have had both eyes enucleated. The onset very soon after removal of the second eye and at the age of 26 years, as well as its practically stationary course for 16 years, strongly suggests the manifestation of a psychic trauma in a hypersensitive individual. Had the cause been a cicatrix, neuroma, or other condition of the optic nerve or brain, the white vision would have had other clinical characteristics. There is no specific cure. Treatment involves (1) the practical care of any ocular or other condition which may be aggravative and increase a tendency to become worse as the patient grows older; (2) physical and, especially, mental hygiene; (3) the experimental use of tranquilizing drugs, which may be of temporary value, especially during periods of stress and emotional upset; and (4) psychiatric treatment with or without hypnosis. The latter treatment is not promising, because of the patient's age and the duration of the white vision sensation.

HOSPITALS FOR PATIENTS ADDICTED TO NARCOTICS

To the Editor:—*Please supply names of hospitals where dope addicts go to be cured.*

V. W. Swayze, M.D., Muscatine, Iowa.

Answer.—Persons who are addicted to opiates or the synthetic equivalents of opiates, marihuana, or cocaine are eligible for admission to the U. S. Public Health Service hospitals at Fort Worth, Texas, or Lexington, Ky. Generally, addicts in areas east of the Mississippi are accepted at Lexington, and those west of the Mississippi are treated at Fort Worth. Information and the necessary blanks for requesting admission can be obtained by writing to the medical officer in charge of either institution. Patients should not go to the hospital until they have been notified that a bed is available. In addition to these federal hospitals, a number of private sanitariums accept addicts, and, in many states, provision for treatment in one of the state mental hospitals can be made. Information must be obtained by writing directly to the sanitarium or to the head of the state hospital system.

PREVENTION OF INGUINAL HERNIA

To the Editor:—*As medical adviser to an aviation corporation, a physician has been confronted with the fact that, although the pilots and mechanics have passed rigid physical examinations before employment, including careful screening for hernia, a great number of them sooner or later develop hernia. It seems that, with proper precautions in regard to lifting and with regular exercises for strengthening the abdominal muscles, this incidence may be definitely reduced. Is there any simple pamphlet of information and instruction along these lines which could be made available to these employees so as to help prevent this situation in the future?*

Paul E. Adolph, M.D., Wheaton, Ill.

Answer.—It is assumed that the inquirer refers to inguinal hernia. This consultant knows of no pamphlet that can be procured with instructions on exercises or precautions for preventing the development of such hernias. Unfortunately, most inguinal hernias developing later in life or those of the direct type result from gradual wearing out of the transversalis fascia. Exercises would be of little value in preventing such hernias, but the avoidance of obesity, as well as attention to any symptoms of urinary obstruction, would aid in reducing their occurrence. A good erect protrusion also is of some help as an aid in protecting this area, as the so-called shutter action on the conjoined tendon.

EFFECT OF DECREASED OXYGEN ON BRAIN CELLS

To the Editor:—*What effect does difficult breathing, causing oxygen lack, and cyanosis have on the brain cells, with special reference to severe, chronic bronchial asthma of many years standing?*

J. M. Hesser, M.D., Benson, Ariz.

Answer.—In patients with chronic asthmatic dyspnea and cyanosis of moderate degree, the brain cells, in all probability, have become acclimatized to oxygen-want and are therefore not damaged. However, in acute, severe asthmatic dyspnea, in which the arterial oxygen saturation declines to very low levels, pathological changes in the brain may take place. The cortex, especially the frontal lobe cortex, is the most oxygen-sensitive organ. With more severe hypoxia, the medulla may be involved, with adverse effect on the respiratory center. The relative sensitivity of various parts of the brain to lack of oxygen was described by Morrison (*Arch. Neurol. & Psychiat.* 55:1, 1946). The effects of hypoxia due to high altitude, as well as respiratory disease, are reviewed by Barach (Physiologic Therapy in Respiratory Disease, Philadelphia, J. B. Lippincott Company, 1948).

TOXICITY OF NEOMYCIN

To the Editor:—*A patient developed motor paralysis of both legs and loss of sensation in both hands after intramuscular injection of neomycin. 1. Have neurological complications to neomycin been previously reported? 2. Do such complications usually affect more prevalently the central nervous system or the peripheral nervous system? 3. Are the sensory or the motor nerves prevalently affected by these complications? 4. Is a written permit from the patient or his next of kin necessary before injection of neomycin? 5. Is a skin test for allergy necessary in order to avoid the dangers of neurological complications due to neomycin?*

Conrad M. Ayres, M.D., New York.

Answer.—1. The neurological complications due to neomycin have been those which affect the eighth cranial nerve in a way similar to those produced by streptomycin and dihydrostreptomycin. 2. Neither the central nervous system nor the peripheral nervous system is affected except as mentioned above. 3. The sensory and motor nerves are not affected. 4. A written permit is not necessary; however, it would be desirable to explain that neomycin may affect the eighth cranial nerve and may have an effect on the kidneys. 5. An allergy skin test is not necessary.

THYROID MEDICATION AND MYOPIA

To the Editor:—*What results are to be expected in giving thyroid medication to adolescent children for progressive myopia? What long-term effects on thyroid function or other endocrine functions are to be expected from long continued use of exogenous thyroid supplied in this manner?*

M.D., Montana.

Answer.—Thyroid medication has been tried without success in the treatment of progressive myopia in children and young adult persons. Its use for this condition is not recommended. Desiccated thyroid substance given in a physiologic dose of 1 to 2 grains (0.06 to 0.13 Gm.) per day will inhibit the production of thyrotropin by the pituitary gland. It may be that, if suppressive doses of this hormone are given for a sufficiently long time, the thyroid gland will be incapable of functioning normally when use of the medicament is stopped. However, in the vast majority of patients who have been given large doses of thyroid substance over a good many years, the gland resumes normal function when treatment with the hormone is stopped. Transient hypothyroidism may follow while the thyroid gland is recovering from suppression.

ANEMIA DURING PREGNANCY

To the Editor:—*A 25-year-old woman is due to have her baby in four months. Her hemoglobin level is 9.5 Gm. per 100 cc. She has received the usual dosage of iron (ferrous sulfate) daily for the past two months. Does this low level of hemoglobin justify a blood transfusion? What hemoglobin level warrants a transfusion in a pregnant woman? There is no reason to believe that the low level in this case is due to blood loss, although the only test done has been a stool examination for occult blood. Presumably the cause is nutritional.* *M.D., Connecticut.*

Answer.—A transfusion of whole blood is rarely justified at this stage of pregnancy. A hemoglobin level of less than 10 Gm. per 100 cc. at or near term is the usual criterion for a transfusion. Iron deficiency is the most common cause of anemia during pregnancy. If orally given iron has failed to raise a low hemoglobin level after a two-month period, it is reasonable to assume that the patient is not absorbing or utilizing the iron. A combination of iron and cobalt might prove effective. If there is reason to suspect that the patient has not taken the prescribed medicament, intramuscularly administered iron would solve the problem.

EPILEPSY AND DIPHTHERIA

To the Editor:—*Could epilepsy develop as a result of a diphtheria infection?*

H. Harris, M.D., Hartford, Conn.

Answer.—There are no references available on development of epilepsy as a result of infection by Corynebacterium diphtheriae. If involvement of the nervous system occurs, it usually is a toxic neuritis or polyneuritis with consequent motor paralysis. Convulsive seizures are not a characteristic manifestation of diphtheria.

EXCESSIVE UNDERARM PERSPIRATION

To the Editor:—*Is there any effective treatment for excessive underarm sweating? This situation is most distressing to several teen-aged patients. Anticholinergic drugs, applied locally as creams and given orally, have been tried with little success.* *Norman R. Bates, M.D., Vashon, Wash.*

Answer.—This problem appears to have no satisfactory solution at present. The proprietary antiperspirants are really quite good, on the whole, and a try of a variety of them is worthwhile. A 10% formaldehyde solution in rubbing alcohol might be tolerable and efficacious; however, it irritates some persons, especially blonds, and its odor is objectionable. Some dermatologists (not all) will countenance x-ray therapy in doses of 300 r at about 120 kv. without added filtration at intervals of two weeks until a total dose of 1,800 r may be reached; this consultant does not recommend it. Phenobarbital is to be considered for occasional use.

EROSION OF THE CERVIX

To the Editor:—*If the results of a Schiller's test are chronic ulcerative cervicitis or chronic ulcerative cervicitis with squamous cell metaplasia, what are the therapeutic indications for patients in their forties with such disease? Please give the indications for hysterectomy in these cases.*

M.D., Illinois.

Answer.—Erosion of the cervix, per se, is no indication for hysterectomy in patients in their forties. Tissue examiners in any hospital will question the need for hysterectomy in such cases unless there are other complications, such as fibromyomas, excessive uterine bleeding, endometrial polyps, adenomyosis, endometriosis, or other pathological disorders. Advantage may be taken of Papanicolaou smears for cancer detection as an aid to the other techniques.

COMPOSITION OF EARWAX

To the Editor:—*What is the chemical composition of cerumen (earwax)? What are the best solvents to use in softening this prior to removal or irrigation? Have the common household detergents been applied as possible solvents?*

M.D., Wisconsin.

Answer.—Cerumen is a mixture of the secretory products of the two glands in the cartilaginous portion of the external auditory canal: sebum from the sebaceous gland, and apocrine sweat from the ceruminal gland. Desquamated epithelial cells, dust, and shed hairs are mixed into the cerumen Tap water, 1 to 2% saline solution, and 1.5 to 3% hydrogen peroxide provide a rapid disintegrating effect on cerumen. In this connection, solutions of some of the common household detergents have been used.

CARCINOMA OF THE BREAST

To the Editor:—*Are there any tests available to determine whether a patient with metastatic and diffuse cancer of the breast will respond favorably to oophorectomy, adrenalectomy, or hypophysectomy?* *M.D., Kentucky.*

Answer.—There are no simple tests available. The details of provocative testing to determine which type of hormone will or will not stimulate a breast cancer are described in the monograph by Jessiman and Moore (Carcinoma of the Breast, Boston, Little, Brown & Company, 1956).

WASHINGTON NEWS

FROM THE WASHINGTON OFFICE OF THE AMERICAN MEDICAL ASSOCIATION

A. M. A. Witnesses Oppose Forand Bill at House Hearing . .
Folsom Explains Value of U. S. Grants-in-Aid Programs . .
A. M. A. Renews Stand on Service-Connection . .

A. M. A. TELLS COMMITTEE REASONS FOR OPPOSITION TO FORAND BILL

During a week of concentrated hearings on social security, when scores of proposals were made for liberalizing all aspects of the program, American Medical Association witnesses explained to the House Ways and Means Committee why most professional associations are opposed to the Forand bill, which provides hospital-nursing home care for social security beneficiaries.

The second week of hearings brought out testimony in opposition to the Forand bill from insurance, chamber of commerce, and other groups and support from organized labor and a few individual congressmen. Most of the questioning of witnesses on the Forand bill was conducted by the bill's sponsor, Rep. Aime J. Forand (D., R. I.), part of the time as acting chairman in the absence of Chairman Wilbur Mills (D., Ark.).

Dr. Leonard Larson, an A. M. A. trustee speaking of the Forand bill, said, "Today you have before you proposals which would . . . mean a federally financed and federally controlled system of medical and hospital care, first for social security beneficiaries, subsequently for other groups, and ultimately for everyone." He said the medical profession is "acutely aware" of the existence of medical care problems among the aged, and he added:

"We do not agree, however, with the advocates of the pending legislation, as to the nature and extent of the problems, or as to the means of solving them. We feel, as do many others, that traditional voluntary private methods can eliminate existing deficiencies and at the same time preserve individual and community freedom."

Dr. Larson then reviewed the progress of medicine, and said "progress through the private enterprise approach is evidence that federal intervention is not required." He also noted the impressive record established by voluntary health insurance of all types. Regarding medical progress and the increasing number of aged, he said:

"Thus we in medicine have helped to create not only the problem of the aged, we have helped to create the aged. We have done it under the free choice system. We can solve the problems in the same way."

At the outset of his testimony Dr. Frank Krusen of the Mayo Clinic made it clear that the A. M. A. "has not in the past and is not now taking a position in opposition to the over-all social security program. . . . However, the (Forand bill) and other recent proposals . . . represent in our opinion a major and dangerous deviation from the original concept of the system."

He then made these points, among others:

1. The aged, for the most part, do not need short stays in general hospitals but rather improved home and community care "as well as less costly and improved chronic illness and nursing home facilities."
2. Under the Forand bill the government would finance health care of 12 million to 13 million persons through compulsory taxes, would control disbursement of funds, would determine benefits and set rates of compensation, would audit and control records, and would establish and enforce standards of hospital and medical care.
3. Beneficiaries would not have free choice of hospitals and physicians.
4. Federal regulations would be imposed on patient and physician alike.
5. Medical efforts alone will not solve the problems of the aged; many other segments of our society will have to contribute. "Many of their ills are the direct result of the inferior role in which this group has been placed. . . . We as physicians are going to find out what the aged really need, what new improvements are succeeding in giving them better health care, and how such procedures can be universally applied."

Dr. Krusen then explained all the efforts of organized medicine to improve the health care of the aged, including sponsorship of the Joint Council to Improve the Health Care of the Aged and support for legislation to help nursing homes obtain mortgages on reasonable terms.

Speaking for the Health Insurance Association of America, E. J. Faulkner opposed the Forand bill for these major reasons: The service benefits are a radical departure from cash benefits and "would seriously jeopardize the system"; the bill would not alleviate the only real problem, the presently aged who are indigent or close to indigent; it would mean a heavy and unnecessary tax; and voluntary health insurance is rapidly solving the problem of the health care of the aged.

Mr. Faulkner was sharply challenged on some of his statistics by Mr. Forand, who produced personal letters and reports that he said underscored the seriousness of the problem.

John H. Miller, for the American Life Convention, also opposed the Forand bill, in general for the same reasons cited by Mr. Faulkner. He said it represents "an initial step in the field of compulsory federal health insurance," a system that would "seriously cripple or destroy the institution of voluntary health insurance."

Edward H. O'Connor, for the Insurance Economics Society of America, concentrated his criticism on the bill's excessive and unpredictable taxes and the regulatory power over medicine that it would lodge in the federal government.

Other Forand critics included A. D. Marshall, for the U. S. Chamber of Commerce, and George H. Frates, Washington representative of the National Association of Retail Druggists. Mr. Forand, attacking the Frates testimony, said the aging people now do not get medical care, and "you should read my mail" to learn this. Asked if his organization had "succumbed to the pressure of the A. M. A.," Mr. Frates replied, "I don't think so. We work with the A. M. A. on some things and oppose them on others."

In a discussion with Mr. Marshall, Mr. Forand said, "I'm sure we are all aiming at the same general goal but can't agree on the method."

Those supporting the Forand bill included spokesmen for hotel service and similar unions, Americans for Democratic Action, and Rep. James Roosevelt (D., Calif.). Mr. Roosevelt has a number of bills to liberalize social security, the cost of which would be about 7 billion dollars annually. Rep. John Byrnes (R., Wis.) remarked that "There aren't the necessary seven billion lying around in the hands of the taxpayers."

FOLSOM EXPLAINS VALUE OF GRANTS-IN-AID

Secretary Marion Folsom of the Department of Health, Education, and Welfare has told Congress that sound federal grants-in-aid can be a force strengthening state governments and preserving and enlarging state responsibilities. He spoke at a House government operations subcommittee which has been conducting a long series of hearings on federal grants and federal-state relationships.

Mr. Folsom cited the "stimulating effect" of federal grants upon state and local financial support for health programs. Between 1947 and 1956 local expenditures for community health rose from 100 to 310 million dollars, for control programs for venereal disease, tuberculosis, cancer, etc. "During this same period federal funds remained at approximately the same level. The federal share therefore decreased from 32 to 14%. The large increase in state and local financing at least partially results from the stimulatory effect of the original federal grants," Mr. Folsom declared.

"There has been a similar increase in state and local support including private support of needed hospital construction, and this increase, too, has been to some degree, at least, stimulated by federal grants. States and localities have matched dollar for dollar federal expenditures to survey the needs for hospital construction in each state, and they plan programs to meet these needs. The health facility needs as disclosed by these surveys have resulted in the raising by states and localities of between two and three dollars for every construction dollar granted by the federal government."

These examples, Mr. Folsom added, support "my strong personal conviction that the interests of our people can be well served by mutual sharing of governmental responsibility through the grant-in-aid device."

The secretary conceded that this approach has its dangers, too. "It can be mistakenly substituted for action that should be taken by the states or local governments, or by business, private organizations, or individuals. And, once used to initiate a program, it is not subject to easy termination.

"While we continue to explore alternative methods for encouraging greater state and local responsibility and participation in programs of social and economic improvement, it is essential that we work to maintain and increase the effectiveness and the efficiency of the existing federal grant-in-aid programs which have a continuing high priority of national interest."

A. M. A. REITERATES STAND ON VA SERVICE-CONNECTION

The American Medical Association has informed Congress that every effort should be made to insure that service-connected cases are not relegated to the background in the Veterans Administration hospital picture, despite a dwindling of such cases to only 15% of admissions. Dr. F. J. L. Blasingame, A. M. A. general manager, made the point in a letter to the House Veterans Affairs Committee. The latter is considering a number of bills that would establish presumption of service connection for a large range of diseases and conditions or would extend already established periods.

"We have always been opposed to the determination of service-connection of diseases and disabilities by legislative enactment. We believe that the question of whether a given disease in a given individual is a result of or was aggravated by military service can only be properly answered on the basis of the facts of the individual case. There are many factors which must be determined and weighed on the basis of the actual case history of the individual before service-connection can be accurately determined.

"It is our belief that the only true mission of the Veterans Administration's Department of Medicine and Surgery is to provide medical care for veterans with service-connected ills. Nevertheless, as long as non-service-connected cases are legally eligible under the present laws, we believe that every effort must be made to insure that service-connected cases, which have now *dwindled to a mere 15%* of annual hospital admissions, do not become relegated to the background of the VA hospital picture."

Appearing in support of one or more of a variety of bills in this area were the Disabled American Veterans, the American Legion, and the AMVETS.

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THIRTY YEARS OF PROGRESS IN THERAPY FOR PARALYSIS AGITANS (PARKINSON'S DISEASE)

Lewis J. Doshay, M.D., Ph.D., New York

The outlook for patients with paralysis agitans is much brighter than it was 30 years ago. There are, however, so many symptoms to treat in the three types of Parkinsonism that many drugs are required. Intensive research should make it possible to discover drugs that will act on the same brain centers as chlorpromazine does, but with the opposite effect of preventing, or permanently arresting, any progression in the symptoms. Surgical procedures are being applied with greater skill and better understanding, and they harbor brighter prospects of relief to the patients.

FROM SMALL beginnings of labor and turmoil in the third decade of this century into the meaning of and prospects for treatment of paralysis agitans (Parkinson's disease), an impressive armamentarium has evolved, along with clearer understandings of the nature and management of the disease and, lately, foundations to promote and support research. The Spanish influenza epidemic of 1918 brought so many cases of epidemic encephalitis (lethargic encephalitis, Economo's disease) that feverish efforts throughout the world became concentrated on discovering a vaccine that would prevent the terrible disease and its sequelae of Parkinsonian symptoms. The endeavor failed, and, by 1928, the aim was diverted toward finding measures that would effectively combat the symptoms.

The task was not easy and was made more difficult by premature and overenthusiastic claims and reports from different areas of the world of remarkable "cures" and remedies for all the symptoms of paralysis agitans, regardless of type or stage. For example, 95% of such patients were being returned to work by treatment with the "miracle drugs." Time and further observation led to a sober reevaluation of the claims, and the pendulum swung the other way. Mass disappointments in medicinal therapy among the doctors and patients brought neurosurgery to the forefront as a possible solution to the inexorable onslaught of the symptoms. Every segment of the brain, spinal cord, and roots was severed. Claims by some investigators were unsubstantiated by others. In the absence of knowledge as to the areas and pathways responsible for tremor and rigidity, the surgical efforts were destined to failure, and they were abandoned by 1945.

From the Department of Neurology, Columbia University College of Physicians and Surgeons, and the Parkinson Laboratory of the Neurological Institute, Presbyterian Hospital.

The past decade witnessed a resurgence of medicinal remedies, spearheaded by synthetic compounds, to replace the time-worn natural (solanaceous) drugs of belladonna, atropine, and hyoscine hydrobromide, which harbored disturbing side-reactions and were, moreover, unsuited to the older patients because of the hazard of glaucoma.

Chemotherapy

The synthetic drugs for the treatment of paralysis agitans had scant reception until it became universally recognized that trihexyphenidyl (Artane) hydrochloride[1] possessed all of the virtues of the potato plant compounds without their disturbing side-effects. Thereafter, pharmaceutical houses competed sharply to produce the best and most widely accepted agents against paralysis agitans. Even so, out of the hundreds of new compounds tested during the past decade in the Parkinson Laboratory of the Neurological Institute, in the Vanderbuilt Clinic, and in private patients, only five others—cycrimine (Pagitane) hydrochloride,[2] procyclidine (Kemadrin) hydrochloride,[3] benztropine (Cogentin) methanesulfonate,[4] ethopropazine (Parsidol) hydrochloride,[5] and orphenadrine (Disipal) hydrochloride[6]—successfully withstood the test of a large series and of long-term study as specific additions to the armamentarium of this disease. (References are provided for those who are as yet unfamiliar with the dosage, uses, and actions of these relatively new drugs.)

There are, however, so many symptoms to treat in the three types of Parkinsonism (postencephalitic, idiopathic, and arteriosclerotic), with rigidity, contractures, muscle cramps, tremors, sialorrhea, oculogyria, akinesia, somnolence, adynamia, akathisia, anorexia, excess sweating, dysarthria, dysphagia, insomnia, agitation, and depression, that many drugs are required. For the purpose, supplementary synthetic agents have become available to the doctor, such as amphetamine, dextro amphetamine sulfate, chlorpromazine (Thorazine) hydrochloride, prochlorperazine (Compazine) ethane disulfonate, promazine (Sparine) hydrochloride, phenaglycodol (Ultran), meprobamate (Equanil), reserpine, diphenhydramine (Benadryl) hydrochloride, phenindamine (Thephorin) tartrate, and others.

Neurosurgical Therapy

Within the past five years active interest in neurosurgery has been revived, but this time the attack by all participants has centered on the basal ganglions. Some favorable, though transient, results have been achieved in younger patients suffering from unilateral symptoms.[7] Such cases, however, can be successfully managed by medicinal therapy. The older patients, who through the years accumulate the worst forms of bilateral symptoms and are highly sensitive to all drugs, are the ones in greatest need of help from surgery. Unfortunately, these are the very ones the neurosurgeon avoids, because of the risks of hemorrhage and other complications. In November, 1957, explorations were begun with a new ultrasonic surgical technique,[8] which may circumvent these risks because the brain and its membranes are not entered. Only time will tell whether it will be suitable to patients within the older age bracket and whether the hoped-for benefits will be of a lasting nature.

As of this writing, two foundations for paralysis agitans are in the process of formation: the Parkinson's Disease Foundation, with its goal geared to research into the cause and means of prevention of the disease, and the National Parkinson Foundation, which plans to promote research into better remedies and facilities for the afflicted. Either or both of these organizations will find comfort in the fact that during the past three years it has been possible to produce the symptoms of paralysis agitans with chlorpromazine and other compounds in persons who never had the disease.[9] Hence, intensive research should make it possible to discover drugs that will act on the same brain centers as chlorpromazine does, but with the opposite effect of preventing or permanently arresting any progression in the symptoms.

Conclusions

All in all, the outlook for patients with paralysis agitans is much brighter than it was 30 years ago. There have been no further attacks from the virus that produced epidemic encephalitis and paralysis agitans three decades ago. There is a much wider and safer selection of drugs with which to combat the symptoms of idiopathic and arteriosclerotic cases. Surgical procedures are being applied with greater skill and better understanding, and they harbor brighter prospects of relief to the patients.

Lastly, there is increasing public and governmental interest in the problems of the aged, and two foundations for the study of this disease have recently been established, one to promote research into the cause and prevention of the disease and the other to study improved measures for the care and rehabilitation of the afflicted.

710 W. 168th St. (32).

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INCREASING THE EFFECTIVENESS OF GOLD THERAPY IN RHEUMATOID ARTHRITIS

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A logical basis for aurotherapy in rheumatoid arthritis is found in a study of the rate of urinary excretion of the injected gold. A total of 138 urinary excretion assays for gold were made in patients who were being treated with intramuscular injections of gold sodium thiomalate or aurothioglucose at different dosage levels. The results confirmed the findings of previous workers that the amount of gold excreted was greater, the greater the amount administered. The highest rate occurred on the day of injection, and about one-seventh of the quantity injected was excreted in the first week. Since individual patients differed in their excretion rates for gold, any fixed dosage schedule must result in toxic symptoms in some and therapeutic failure in others. Toxicity to gold salts was found not to be a serious hazard. It was reversible, and its appearance was a criterion for the adequacy of the dosage. A comparative study of 347 patients showed that individualized programs of therapy were more effective than standard programs. Individualized programs induced remissions in 82% of the cases. The remissions occurred after 12 to 18 weeks of treatment and were made lasting by continuing the dosage at a maintenance level for eight months.

No method of treatment has proved capable of producing complete and permanent remissions of peripheral rheumatoid arthritis in all cases. In fact, only aurotherapy (chrysotherapy) has been successful in permanently arresting the disease with any consistency. The controversy surrounding aurotherapy in the treatment of rheumatoid arthritis has raged for more than 30 years, since the first published reports of its use appeared in 1927.[1] The lack of uniformity in reporting the results of treatment, ranging from "cure" through "marked improvement," "moderate improvement," and "slight improvement" to "no benefit," as well as variations in the program of dosage, has done nothing to resolve the wide divergence of opinion. Nevertheless, most investigators who have given gold therapy an adequate clinical trial have admitted that it has been an effective agent in the treatment of rheumatoid arthritis.[2] It is now apparent that the number of remissions were probably kept to a minimum because of methods of administration, predicated almost entirely on an attempt to develop a program of gold therapy which would eliminate toxic reactions. In other words, group therapy was the goal rather than individualized treatment schedules.

The gamut of dosage has been run, including course therapy, interrupted by rest periods, course therapy followed by maintenance therapy, and low safe-dose therapy.[3] Cure or complete remission has been reported, varying from 9.9%[3a] to 54%.[2e] Un-

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From the Benjamin Franklin Clinic.
Read in part before the International Congress of Rheumatic Diseases, Toronto, Canada, June 24, 1957.

fortunately, many of the higher figures were scaled down later when relapses occurred, but over-all permanent benefit was in the vicinity of 33%.[2c] If gold therapy can produce a complete remission without relapse in approximately one-third of the patients treated,[2f] why not in all and why not permanently? This paper is presented as a positive answer to this question.

Definitions

A remission of rheumatoid arthritis, for the purpose of this report, is defined as the complete subsidence of the inflammatory joint disease as well as the disappearance of all those systemic effects which are still reversible, including elevated sedimentation rate, anemia, weight loss, iritis, and circulatory deficiencies. A remission cannot be construed to include restoration of severely damaged joints to normal, correction of deformities, complete disappearance of thickened periarticular tissues, or rehabilitation of atrophied muscles. A successful remission should continue for at least five years after therapy has been discontinued.

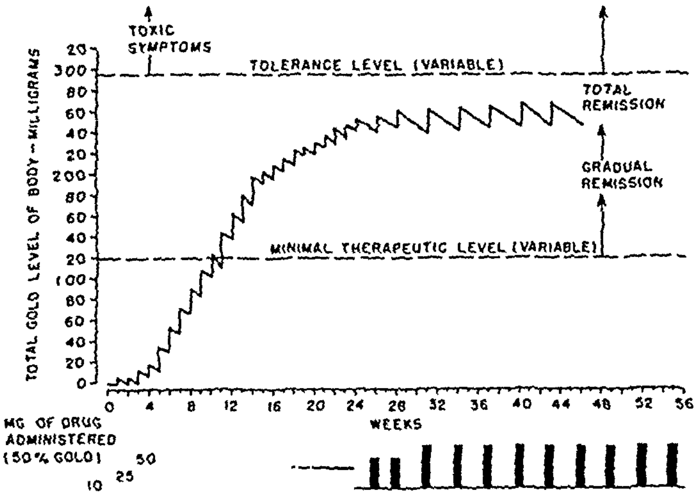

Fig. 1.—Theoretical basis for gold therapy (excretion rate of gold, 1 mg. per day).

Some confusion may exist in the minds of many people in regard to the meaning of gold, gold salts, and gold therapy. It should be understood that a gold preparation injected for the treatment of rheumatoid arthritis contains 50% or less of gold. Disodium aurothiomalate (Myochrysine) and aurothioglucose (Solganal) have a 50% gold content, while gold sodium thiosulfate contains 37.5% gold. All three of these preparations are soluble gold compounds. For the comparison of injected gold with the excretion rate, the gold content alone will be considered and designated as, for instance, 25 mg. of gold or 10 mg. of gold. When the injected preparation is mentioned, it will be indicated as gold salts or by the generic name. Only those preparations containing 50% of gold have been studied and reported in this paper.

Theoretical Basis for Gold Therapy

Freyberg and co-workers[4] have shown that patients receiving 50 mg. of soluble gold (100 mg. of a soluble gold salt) every week have an average daily urinary excretion of approximately 0.7 mg. Since some gold is lost in the feces and probably some through perspiration and other means, an arbitrary average total value of 1 mg. for the 24-hour excretion rate was assumed for practical guidance in treating our patients. This figure was used to calculate maintenance dosage, as well as to determine the approximate amount of gold remaining in a patient's body at any given time. The last consideration is very important when reinstituting aurotherapy for treatment during a relapse, that is, for calculating the approximate amount of gold salts which will be required to achieve the level necessary to reproduce a remission.

Experience has dictated that the placing of an arbitrary ceiling for amount of gold to be given at a total number of weekly doses or at a total number of milligrams of the drug is detrimental to the best interests of the patient. Indeed, the total number of milligrams administered is a competely false figure, since only the gold which remains in the body is of any consequence. Granting the fact that 1 mg. excreted daily is only an average arbitrary figure, for practical purposes it seems to permit calculations which approach the actual level and is more realistic than the total amount of drug administered.

The aims of aurotherapy are (1) to build a level of gold in the body of the patient sufficient to produce a remission and (2) to maintain that level until a permanent remission is established. Although it is desirable to secure this beneficial effect without the development of a toxic reaction, it is a well-established fact that when toxicity occurs the rheumatoid arthritis is quiescent.[2f] The corollary is also true: patients who fail to receive benefit from aurotherapy do not experience toxicity.

If all of the previous assumptions are correct and if there is an average daily excretion of gold, the total amount of gold in the body immediately after an injection gradually declines until the time of the next injection. Figure 1 shows the theoretical course in a patient responding to an average treatment program. An average treatment program consists of 24 weekly injections of aurothioglucose or disodium aurothiomalate, 10 mg. for 2 weeks, 25 mg. for 2 weeks, 50 mg. for 10 weeks, and 25 mg. for 10 weeks (an alternate program for the last 20 weekly doses has been 50 mg. per week) followed by 35 mg. every two weeks and then 45 to 50 mg. every three weeks for eight months after all rheumatoid activity has ceased. As the total gold level increases, the majority of patients will begin to show some improvement. This is the "minimal therapeutic" level, which varies from patient to patient. Further elevation of the total gold level tends to increase the improvement to the point of complete remission. If the weekly injections of 50 mg. of the gold salts are continued, a toxic reaction is apt to occur in four to six weeks, an indication that the patient's tolerance level has been surpassed and that the aurotherapy should be temporarily discontinued. During the time that treatment is interrupted, the excretion continues at the same rate of 1 mg. daily, the total gold level gradually decreases, and, when it drops below the tolerance level, the toxic reaction clears. Gold excretion should be permitted for an additional two or three weeks before a maintenance program is instituted, to allow a margin of safety against another toxic reaction which otherwise may occur with any future elevation of the gold level.

A successful remission must be continued for approximately eight months to prevent an exacerbation of the rheumatoid activity after discontinuance of the aurotherapy. The maintenance dosage should be adjusted to replace the amount of gold lost by excretion between injections without materially increasing the total gold level. Therefore, an average maintenance dose at two-week intervals of 35 mg. of a 50% gold salt (17.5 mg. of gold) replaces the 14 mg. lost by excretion and provides an excess of 3.5 mg. The dosage required every three weeks is 45 to 50 mg. (22.5 to 25 mg. of gold). This will replace the 21 mg. lost, with an increment of 1.5 mg. to 4 mg. Theoretically, longer intervals between 50-mg. injections of the drug would be inadequate maintenance therapy.

The observation that an occasional patient developed a transient dermatitis with each injection (tolerance level surpassed by a few milligrams) or other patients tended to relapse (total gold level gradually falling) after they had been on maintenance therapy for several months led to the hypothesis that there must be considerable variation in the urinary excretion of gold, that is, an average excretion of less than 1 mg. in the first instance and greater than 1 mg. in the latter. In addition, the extreme variation in patient response to a standardized program of aurotherapy suggested wide differences in either the tolerance levels or the urinary excretion rates. Since no known method for determining the tolerance level of gold, short of producing a toxic reaction, was available, the possibility of variations in the excretion rates for gold assumed increasing importance. Consequently, it became imperative to study urinary excretion rates for gold in an effort to prove or disprove this theoretical basis for gold therapy which stemmed from clinical observations and impressions.

Materials and Methods

The urinary excretion of gold was studied in patients who exhibited clinically (1) an excellent therapeutic response to aurotherapy (normal excretion), (2) relapse during maintenance therapy (hyperexcretion), (3) low tolerance for gold salts (hypoexcretion), and (4) little or no response to an average gold therapy program (hyperexcretion).

All patients were instructed to empty the bladder just before receiving an intramuscular injection of gold sodium thiomalate or aurothioglucose. Collections were then made every 24 hours for the next seven days. The total volume was measured, and an 8-oz. aliquot was taken for assay. The total daily excretion and the total excretion for one week were determined by the method of Block and Buchanan.[5] The gold salts, disodium aurothiomalate and aurothioglucose, were used interchangeably in the first series of 140 patients (those receiving a standardized program of therapy with 1,070 mg. of gold salts in 24 weeks). However, irregularity of dosage often occurred with the latter compound, a suspension, if it was not thoroughly shaken to resuspend the particulate matter which settled out on standing. The disodium aurothiomalate, a true solution, could be measured with accuracy. The recent addition of a 10-cc., rubber-stoppered, multiple-dose vial, each cubic centimeter containing 50 mg. of the salt in solution, has overcome the problem of wastage which occurred with doses other than 10 mg., 25 mg., and 50 mg., which are the standard concentrations in the single-dose ampuls. A new concentration, which has been under clinical investigation, of 100 mg. per cubic centimeter in a 10-cc. multiple-dose vial is a further improvement. It is considered superior since it permits a minimum quantity of material for injection of any desired dose, as well as insurance against wasting of material.

Table 1.—*Sample Comparison of Dosage and Excretion of Gold Salts in One Patient*

Dose of Gold/Wk., Mg.	Length of Therapy, Wk.	Excretion/Wk.	
		Total, Mg	%
5.0	1	0.74	14.80
	2	0.69	13.80
12.5	2	1.75	14.00
25.0	1	3.56	14.20
25.0	6	3.53	14.12

All of the 207 patients in the second and third series (those receiving a standardized program of therapy with 820 mg. of gold salts in 24 weeks and those on individualized programs, respectively) were placed on therapy with disodium aurothiomalate. Six patients (2.8%) were changed to therapy with aurothioglucose because of repeated "nitritoid" reactions. No change of gold preparation was required in four patients (1.9%) who had one to three mild nitritoid reactions; these reactions were transient and did not recur.

A total of 138 assays confirmed the findings of Freyberg and co-workers[4]: "The excretion of gold increased as larger amounts of gold were injected," and "the excretion of gold did not increase after the amount of gold injected was no longer increased" (table 1). In general, the excretion of gold was greater on the day of injection, but exceptions were found when the excretion was greater in the second 24-hour period and, in some instances, in the third, fourth, or fifth 24-hour period.

Excellent Response.—Those patients who exhibited a normal response to aurotherapy, that is, remission of the arthritis, excreted approximately one-seventh ± 0.14 mg. of the dose of gold during the week after its administration, which is comparable to the results reported by Freyberg and associates [4a] for patients receiving 25 mg. of gold per week. Compare the dose of gold injected with the total excretion multiplied by a factor of seven in table 2 (cases 1 and 2). The findings tended to be slightly higher during the first week after the dose of gold salts was increased but fell within the range of one-seventh ± 0.14 mg. of the injected material when the larger dose was continued (table 1). The data suggest that up to 85% of the injected gold is retained in the body, less that amount which is excreted in feces, perspiration, and other forms of loss.

Patients with the lowest gold clearance tended to develop a toxic reaction much earlier in the course of therapy.

A toxic dermatitis developed in one patient (table 2, case 5) after he received a total of 70 mg. of aurothioglucose. The dosage schedule consisted of a first and second 10-mg. injection and a first and second 25-mg. injection. The urinary excretion was studied during the week after the first 25-mg. injection. The seven-day excretion, 0.57 mg., was extremely low, in fact, the lowest of any patient studied, amounting to 4.6% of the injected dose or approximately one-third of the quantity of gold which might be expected to be excreted by a patient responding normally to aurotherapy. These findings suggest that there are some patients who have a low tolerance level for gold.

Another patient (table 2, case 6), who developed dermatitis after receiving a total of 820 mg. of gold salts, had been given 10 mg. per week for 2 weeks, 25 mg. for 2 weeks, and 50 mg. for 15 weeks. The urinary excretion was studied during the week after her seventh 50-mg. injection (420 mg. of gold salts). The total excretion for the week was 2.50 mg., only 10% of the injected gold, which was a little more than two-thirds of the expected normal excretion.

TABLE 2.—*Response to Gold Salts Therapy in Ten Patients*

		Excretion, Mg.										
		Daily										
No. of Case	Dose, Mg.	1	2	3	4	5	6	7	Total	% of Dose	Total for Wk. × 7	Remarks
1	5.0	0.17	0.24	0	0.21	0.15	0	0	0.77	15.4	5.39	Normal excretion
2	25.0	1.00	0.75	0.63	0.45	0.12	0.15	0.41	3.51	14.0	24.57	Normal excretion
3	17.5 q. 2 wk.	0.40	0.12	0.15	0.14	0.50	0.22	0.94	2.47	14.1	17.29	Maintenance therapy; normal excretion
4	25 q. 3 wk.	0.28	0.44	0.70	0.65	0.59	0.48	0.41	3.55	14.2	24.85	Maintenance therapy; normal excretion
5	12.5	0.18	0.05	0.09	0.07	0	0.10	0.08	0.57	4.6	3.99	Early toxicity (hypoexcretion)
6	25	1.00	0.25	0.65	0.43	0.05	0.12	0	2.50	10.0	17.50	Early toxicity (hypoexcretion)
7	25 q. 3 wk.	0.64	0.76	0.56	0.67	0.70	0.46	0.49	4.28	17.1	29.96	Relapse during maintenance therapy (hyperexcretion)
8	25	0.73	1.30	2.18	0.41	1.04	1.27	0.18	7.11	28.4	49.77	No response (hyperexcretion)
	50	1.87	1.24	1.06	0.59	0.94	0.98	0.49	7.17	14.3	50.19	Response
9	25	1.60	1.10	1.20	1.10	0.43	0.18	0.46	6.07	24.2	42.49	No response
10	25	0.48	1.34	0.57	1.21	1.17	0.23	0.16	5.16	20.6	36.12	No response

During maintenance therapy in patients showing normal response, regardless of the dose required by a given patient (for example, as in table 2, 35 mg. of gold salts every two weeks for the patient in case 3, and 50 mg. every three weeks for the patient in case 4), the total weekly excretion during the first week after an injection was again within the range of one-seventh ± 0.14 mg. The excretion during the second or third week, after a maintenance dose was given, varied between 15% and 12% of the injected dose. The inconsistency of these findings made them of no value in the present study.

Low Tolerance for Gold Salts.—In each of the three groups of patients who showed abnormal responses clinically, excretion rates were compared with the preceding "normal" excretion rates. Patients who exhibited intolerance to gold salts had excretion rates of less than one-seventh ± 0.14 mg. of the injected gold, indicating hypoexcretion. In fact, there was a rough correlation between total amount of gold salts administered, the excretion rate, and onset of toxicity (table 2, cases 5 and 6).

Relapse During Maintenance Therapy.—The exacerbation of symptoms, during maintenace therapy of 50 mg. of gold salts every three weeks, in patients who had been in complete remission clinically suggested an excessive excretion rate (hyperexcretion). Studies of the gold clearance in this type of patient showed urinary excretions of greater than one-seventh ± 0.14 mg. during the week after an injection. The patient in case 7 (table 2) illustrates these findings. Her total excretion for the week after her maintenance dose during a relapse (fourth month of maintenance therapy, 50 mg. every three weeks) was 4.28 mg., 17.1% of the dose. She was given 50 mg. of gold sodium thiomalate weekly for three weeks. Remission was again apparent after the second weekly dose, but the third weekly injection was given to elevate her total level of gold to provide a safer margin against relapse. Successful maintenance dosage has been 60 mg. of gold salts every three weeks for eight months, after which time the gold therapy was discontinued.

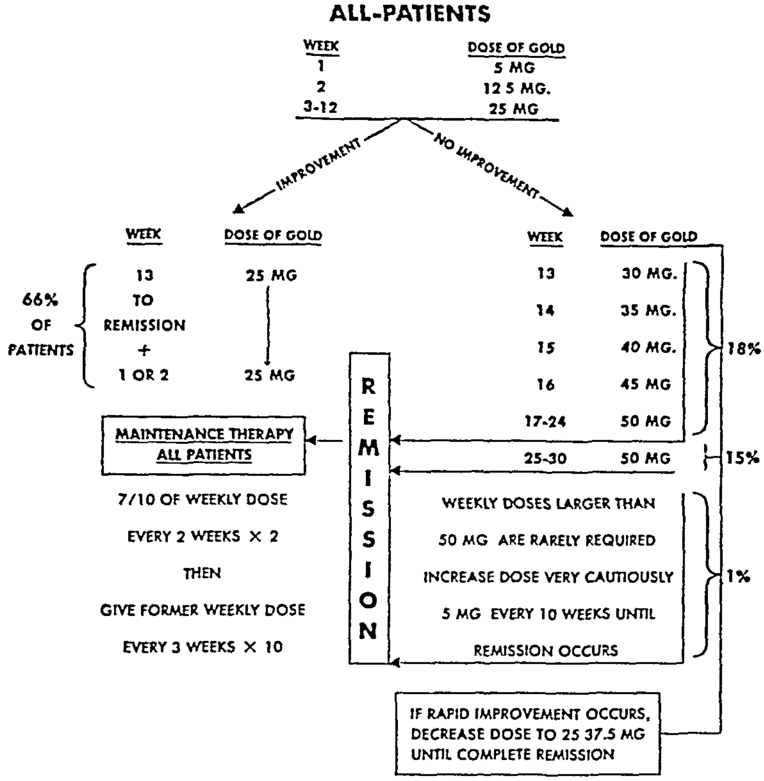

Fig. 2.—Individualized chrysotherapy program (intramuscular injections of 50% gold salts).

No Response to Therapy.—Patients in the final group, those in whom gold therapy is generally considered to be a partial or complete failure, without exception, to the time of writing, have exhibited extremely high excretion rates. The patient in case 8 (table 2) is an excellent example of this type of patient. In spite of the fact that she had received 50 mg. of gold sodium thiomalate for 78 weeks (3,900 mg.) and 50 mg. every two weeks for 18 weeks (900 mg.), she was not in complete remission. Her total excretion for one week was 7.11 mg., 28.4% of the total dose of gold. If this figure is considered on the basis of one-seventh of an injected dose of gold, she would require no less than 50 mg. of gold or 100 mg. of a 50% soluble gold salt. When this dose was administered weekly for 10 weeks, the excretion rate was found to be 7.17 mg. (14.3%). This fell within the range of one-seventh ± 0.14 mg. Remission developed rapidly after the 14th weekly dose of 100 mg. of gold salts. She is now maintained on therapy with 100 mg. every three weeks.

Other examples of excess excretion are as follows (table 2): The patient in case 9, who excreted 6.07 mg. (24.2%) of the dose in one week, received 10-mg. increases of gold sodium thiomalate each week up to 100 mg. and went into remission after 12 weeks of this dose; the patient is now maintained on therapy with 100 mg. every three weeks. The patient in case 10, with an excretion of 5.16 mg. (20.6%) of the dose, needed 100 mg. weekly for 11 weeks to produce a remission and is maintained on 100 mg. of the gold salt given every three weeks.

Therapeutic Considerations

Standard chrysotherapy programs used previously (50 mg. of disodium aurothiomalate from the 5th to 24th week and, in an effort to reduce toxicity, 50 mg. from the 5th to 14th week followed by 25 mg. to the 24th week) have produced complete remissions in 66.4% and 54.0% of patients respectively (table 3). The excretion studies have confirmed the clinical empressions that gold therapy programs must be revised and individualized to secure remissions in the remaining 34% who improved or failed to respond.

The outline for gold therapy as shown in figure 2 is recommended to increase its effectiveness in rheumatoid arthritis.

The comparison of standard chrysotherapy programs with an individualized chrysotherapy program is only pertinent when complete remissions are compared. The categories "complete remission," "improved," and "not improved" of the patients in the standard programs indicate the direct results in patients whose therapy was terminated after a standard maintenance therapy lasting six to eight months in addition to the 24 weekly doses. On the other hand, patients in the individualized program designated as "improved" or "not improved" have not, at the time of writing, completed their therapy but are continuing to follow the program with gradually increasing doses, as outlined previously, until a complete remission occurs.

Table 3.—*Standard Versus Individualized Chrysotherapy Programs*

	Patients in Standard Programs				Patients in Individualized Programs	
	1,070 Mg in 24 Wk		820 Mg in 24 Wk		440-2,800+ Mg in 12 to 30+ Wk	
	No	%	No	%	No	%
Complete remission	93	66.4	66	54.0	70	66.0
Improved	26	18.5	20	16.4	12	14.1
Not improved	21	15.0	36	29.5	3	3.5
Total	140		122		85	

Table 4 shows the distribution of the patients receiving the newer individualized therapy at the present time. The group receiving 440 to 1,120 mg.

includes those patients who showed some improvement by the end of 12 weeks. Those who received 540 to 2,200 mg. showed no improvement at 12 weeks, and, therefore, are given gradually increasing therapy. If complete remission occurs within 24 weeks, maintenance therapy will be instituted. With failure to have a remission in 24 weeks, they can be placed in the group receiving 2,200 to 2,800 mg., and if no improvement is shown by the 30th week with this dosage schedule, they will receive more than 2,800 mg. until remission does occur. Thus, any patient showing no improvement at the end of the given number of weeks will progress into the next group to the right.

Table 4.—*Patients in Individualized Chrysotherapy Program*

	Total		440-1,120 Mg., 12-24 Wk.		540-2,200 Mg., 12-24 Wk.		2,200-2,800 Mg., 24-30 Wk.		>2,800 Mg., 30+Wk.	
	No.	%	No.	%	No.	%	No.	%	No.	%
Complete remission ...	70	82.3	46	65.7	13	18.5	10	14.3	1	1.4
Improved	12	14.1	5		5		2		0	
Not improved	3	3.5	0		2		1		0	
Total	85		51		20		13		1	

These 85 patients have been treated at the Benjamin Franklin Clinic by the "improved chrysotherapy program" with guidance from urinary excretion rates. Included in this group are 26 patients who failed to achieve complete remission on previous gold therapy. There were 15 in whom treatment was considered to be a failure and 11 who had only partial benefit. Every effort is being made to recall all the patients who were unsuccessfully treated previously and enter them into this program.

Precautions in Therapy

Mandatory precautions are as follows: Before each injection the patient must be questioned for itching, rash, or sore mouth; the urine must be examined for presence or increase in red blood cells, albumin, or casts; and the total leukocyte count and the eosinophil count must be checked, because an increase may indicate impending toxicity. Every four weeks a check must be made of the complete blood cell count and the erythrocyte sedimentation rate.

The complete treatment of active rheumatoid arthritis must include, in addition to individual chrysotherapy, (1) pain relief with salicylates and minimal steroid therapy; (2) a rehabilitation program to combat the secondary fibrositis and deformity, including muscle-relaxing drugs, muscle-setting exercises, and intra-articular and extra-articular steroid injections; (3) musculoskeletal supports and shoe corrections when indicated; (4) regulation of rest and activity so as not to exceed the limits of fatigue; (5) antianemia therapy; (6) education in the natural history of the disease to ensure better patient cooperation; and (7) psychotherapy.

Toxicity to Gold.—A toxic reaction is caused by hypoexcretion (hyperretention) and is an indication that the retained gold has exceeded the tolerance level. In patients with hyperretention this reaction may occur with as little as 70 mg. but generally only after 300-500 mg. of the gold salts has been administered (table 2, cases 5, 6, and 7).

The toxic reactions observed in our patients consisted, in order of frequency, of pruritus, dermatitis, stomatitis, leukopenia, and renal changes. Although thrombopenia, toxic hepatitis, and gastrointestinal disturbances have been mentioned in the literature,[6] they have not occurred in our patients. Preexisting renal damage has not been considered a contraindication for gold therapy. In these patients, any increase in the abnormal renal findings is considered to be evidence of toxicity.

It is difficult to anticipate a toxic reaction in patients with extremely low tolerance levels (table 2, cases 5 and 6). Early transient itching of the skin often gives warning that the tolerance level has been surpassed by several milligrams of the gold. In general, toxic manifestations occur within several days after the injection has been given. When moderate doses of gold, and especially when the larger doses, are administered, any rapid improvement in the joint swelling and pain often gives warning that the tolerance level is being approached rapidly.

The toxic reaction is the only absolute clinical measurement of a patient's tolerance level. Since the toxic reaction is reversible on temporary withdrawal of the gold therapy, it is self-limited. Serious symptoms occur when the chrysotherapy is continued in spite of evidences of toxicity. If a *toxic reaction does develop, the* following measures should be taken: 1. Stop gold therapy. 2. Give prednisolone or prednisone, 10-20 mg. daily, and/or steroid lotion, applied locally, for rash (toxic reaction may persist from a few days to more than a month until gold level drops below tolerance level). 3. Two or three weeks after the toxic reaction has

Table 5.—*Toxic Reactions to Gold Salts in Patients in Three Therapeutic Groups*

	Standard Programs				Individualized Programs	
	1,070 Mg. in 24 Wk		820 Mg. in 24 Wk.		440-2,800+ Mg. in 12-30+ Wk.	
Level of Dosage, Mg.	No.	%	No.	%	No.	%
<100	1	0.7	1	0.8	0	0
100-500	12	8.5	11	9.0	7	8.2
500-800	8	5.7	9	7.4	3	3.5
800-1,500	4	2.8	0	0	2	2.4
1500-2,000	0	0	0	0	2	2.4
>2,000	0	0	0	0	1	1.1
	25	17.7	21	17.2	15	17.6

cleared and the steroid has been withdrawn, institute maintenance therapy at two-thirds to three-fourths of the previously planned dose. 4. Reserve dimercaprol for failure of toxic reaction to be symptomatically controlled by steps 1 and 2 (rare). It neutralizes the gold effect (remission), and an exacerbation develops.

The toxic reactions observed in the three groups of patients included in this report are summarized in table 5. A total of 25 patients (17.7%) showed such reactions in the group receiving the standard program of 1,070 mg. of gold salts in 24 weeks, 21 (17.2%) in the group receiving 820 mg. in 24 weeks, and 15 (17.6) in the group receiving the individualized program of therapy.

It is evident that more toxic reactions tend to occur during the earlier phases of treatment. Experience has taught that the development of a complete remission with 50-mg. doses of gold salts tends to be more insidious and, therefore, not recognized, whereas the more rapid type of remission, which is likely to occur when higher dosage schedules are administered, can be a warning signal.

Comment

The inadequacy of determining the limits of a program of aurotherapy should be apparent from the preceding data. The only gold which can be of importance is the quantity remaining in the body; unfortunately, this amount cannot be measured at this time. The therapeutic axiom that the dose of a drug is "enough" becomes a sagacious rule for the use of gold salts in rheumatoid arthritis. Treatment must be individualized and by "touch"; that is, a basic program of therapy may be considered as suitable for the average patient but must be altered as shown necessary by close clinical supervision. When gold salts therapy seems to be failing, increased amounts of gold are indicated up to an actual toxic reaction, at which time a true clinical measurement of an individual's tolerance level has been established and a final successful result can be anticipated.

The fear of the potential toxicity of gold should no longer be the primary contraindication for its use in the treatment of active rheumatoid arthritis. Although a toxic reaction is not necessary in the development of a remission, the complete reversal of the rheumatoid activity continues throughout the duration of the toxic reaction and within a range of 50 to 100 mg. below the tolerance level for gold. The method of determining the urinary excretion rate for gold is so difficult that it does not lend itself for use as a routine laboratory procedure. The gold excretion varies so much from day to day that only total weekly excretion rates are of value. This, too, limits its clinical usefulness, since 24-hour urine collections must be made for seven consecutive days. The method is, therefore, a research tool which has been used to confirm our clinical impressions. In this way, an improved program for chrysotherapy has been devised and tested to include the 34% of patients (table 3) who had shown only some degree of improvement with gold therapy or who exhibited no benefit at all. Employment of the program, as outlined, in patients previously considered unresponsive to gold therapy has proved its utility in producing complete remissions of rheumatoid arthritis.

These studies of the urinary excretion rates for gold have indicated those patients who derived limited benefit or who failed to respond to chrysotherapy because of an increased loss of gold in the urine with little or no variation in the tolerance level. On the other hand, when toxic reactions develop with a very small total dose of gold salts despite a very low excretion rate for gold, there is also an abnormally low tolerance level. Fortunately, this combination of circumstances apparently occurs in less than 1% of patients who receive chrysotherapy.

It can, therefore, be anticipated that, short of a distinct idiosyncrasy to gold, the proper application of an individualized dosage schedule for chrysotherapy, exercising all precautions, will bring about a remission of rheumatoid arthritis. However, the defeat of the "great crippler" is not complete until a total program of treatment is devised for each patient to include, in addition to the specific antirheumatoid chrysotherapy, elimination of fibrositis, correction of anemia, control of psychogenic factors, and restoration of a normal or near normal way of life.

Summary

Studies of total weekly urinary excretion rates of gold have confirmed clinical impressions that variations in patient response to chrysotherapy are due to wide differences in the retention and excretion of gold. When adequate gold salts are administered on a weekly basis, complete remission can be expected in 12 to 18 weeks and will be continued by maintenance therapy for eight months. A new individualized program for chrysotherapy has been successfully employed to procure complete remissions in patients who were formerly classified as having treatment fail or who only improved when treated within accepted limits of gold therapy. The complete remission rate has been increased from 66.4% to 82.3% by employing this method, with every evidence that it will approach closer and closer to 100%. Toxicity to gold salts is not a serious hazard. It is reversible and provides a measurement for reinstituting an adequate nontoxic maintenance dose to secure a permanent remission.

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GOLD IN THE TREATMENT OF RHEUMATOID ARTHRITIS

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Since October, 1932, 3,120 patients with a positive diagnosis of rheumatoid arthritis have been studied. Since 1940, gold salts have been given to all patients with reversible rheumatoid arthritis who were in good health otherwise. The gold salt was given intramuscularly at weekly intervals, the initial dose being 10 mg., then 20 mg., and then 40 mg. weekly. If no signs of sensitivity appeared, treatment was continued until 500 mg. had been given. Use of gold salts affords patients 20% better chance of complete recovery or of major improvement. Severe reaction to gold occurs in a very small percentage of patients.

The motive for this survey was stimulated by the current trend of the increasing use of gold salts in the treatment of rheumatoid arthritis. Also, we were anxious to determine the extent of its effectiveness as part of the complete program in controlling the progression of this type of arthritis when compared with the course of the disease in patients not receiving gold.

Since October, 1932, there have been 3,120 patients with a positive diagnosis of rheumatoid arthritis who had been studied and followed for varying periods of time in our practice. Gold salts have been a valuable agent in treatment in this group since 1933, although in the early years it was not used in the mild cases unless response to other treatment was considered inadequate. However, since 1940, it has been given to all patients with

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reversible rheumatoid arthritis who were in good health otherwise. Individually, the duration of gold therapy varied from one injection to continuous use over a 20-year period and the total amount from 10 mg. to 11,890 mg. administered intramuscularly.

History and Pharmacology of Chrysotherapy

History.—Koch,[1] in 1890, reported the results of his experiments that demonstrated the inhibition of the growth of tubercle bacilli when they were exposed in a gas of gold cyanide. It was one of the harbingers of chemotherapy, and, in 1913, Feldt[2] reported the bacteriocidal properties of certain preparations of gold which contained a sulfhydryl group. In 1927, he[3] demonstrated the effectiveness of gold thioglucose against experimentally produced streptococcic and spirochetal infections in mice. The same year, Lande[4] and Pick[5] independently discussed the effect of gold salt therapy in patients with rheumatoid arthritis, and, in 1928, Forestier[6] began to use it intensively, reasoning that if gold salts were of value in other chronic diseases, such as tuberculosis, they might be effective in rheumatoid arthritis. The first of his several reports appeared in 1929 and provided the impetus for the use of gold salts generally.

Pharmacology.—During the course of weekly intramuscular injections, usually there is 0.4 to 0.8 mg. of gold per 100 cc. in the blood plasma. Approximately 1 mg. is excreted daily, with a range of 7 to 10 mg. per week. After cessation of administration, the presence of gold can be demonstrated in the plasma and urine for a period of 6 to 12 months and may be detectable in the tissues for as long as three years. There is no increase of concentration of gold in the synovial fluid after intramuscular use.

Methods

Criteria.—The criteria for the study included a history, complete physical examination, pertinent laboratory data, and x-ray examination. An individual program was explained in detail to each patient. It consisted of weekly intramuscular injections of gold salts, a minimum initial period of three weeks' complete bed rest, physical therapy (including instructions in exercises), psychotherapy, use of analgesics, sedation, and orthopedic aids, and, when indicated, steroid therapy. Those making up the "control" group were given the same over-all instructions, with the single exception that gold salts were not administered. A few patients received small amounts of Streptococcus vaccine in its place.

Only patients who had been observed weekly for a minimum of three months were included in this study. There were records of 507 patients who received gold salts and 566 control patients. It was decided, further, for purposes of evaluation, to divide the gold-treated persons into groups of those who had received a total of more or less than 300 mg. of gold salts. There were 369 patients who had been given more than this amount and 138 who had received less. This latter group consisted of patients who had manifested sensitivity to gold, who were started on gold therapy recently, or who had discontinued this treatment by their own choice.

For ease of interpretation of data, the severity of the disease was classified as mild, moderate, or severe at the time of the original examination. The standard classification of the American Rheumatism Association could not be used, since many of the patients were first seen prior to its acceptance. The evaluation of the therapeutic response was established from recent progress notes as recorded in the charts.

Method of Administration of Gold Salts.—The gold preparation used generally was gold sodium thiomalate (Myochrysine), but a small group was treated with aurothioglucose (Solganal). The gold sodium thiomalate was procured in a 10-cc. rubber-stoppered, multidose vial containing 50 mg. per cubic centimeter in solution. A new concentration, now under clinical trial, contains 100 mg. per cubic centimeter; this is much to be preferred, since it provides the minimum amount of injected drug in any dose with little or no attendant irritation. Furthermore, the multidose vial provides complete flexibility of dosage without any wastage of material, as is occasioned by discarding unused portions from single opened ampuls.

The gold salt was given intramuscularly at weekly intervals, beginning with a dose of 10 mg., then 20 mg., and then 40 mg. weekly. If no signs of sensitivity appeared, treatment was continued until 500 mg. had been given. At this point, the weekly dosage was determined on the basis of the patient's clinical status. Those with moderate or severe arthritis usually required weekly injections of 40 mg. until 800 mg. had been administered, then 20 mg. for four weeks, 10 mg. weekly for four weeks, 10 mg. at increasing intervals, and, finally 10 mg. once every four weeks for years. Those with mild symptoms were not given as much gold salts after the first 500 mg., since the dosage was cut more rapidly to be leveled eventually at 10 mg. monthly for years. It should be stressed that, during the period of dosage of 10 mg. per month, should exacerbation occur the dose of gold salts given should be increased and the intervals between injections shortened in order to control the symptoms.

The gold was injected into the deltoid muscle, with use of a 24-gauge, ¾-in. needle, which produced no local inflammatory reaction, was well tolerated, and was easier to administer than into the gluteal region. At each visit, prior to injection, the patient was questioned concerning signs of sensitivity, especially glossitis or dermatitis. Complete blood-cell count and urinalysis were done every three or four weeks.

Results of Treatment

The response to therapy between the gold-treated and control patients was compared in order to evaluate the groups as determined by the severity of the arthritis at the initial examination. Table 1 illustrates these details.

Attention is called to the number of patients who had an excellent, or major, response to treatment. An average of 20% more had that grade of improvement in each gold-treated group, which would indicate the effectiveness of gold therapy in rheumatoid arthritis. Another interesting observation is the relatively large number of those with moderate or severe involvement who had excellent or major improvement. This is in contrast to other medical reports in which those with mild involvement had the best results. The reason for this good response in those who had more than mild involvement may be due to the close observation and treatment, extending over a period of many months or years, in this group of private patients.

It should be emphasized, too, that only a relatively small number in each group showed no response to therapy. There are many reasons for this lack of response, such as the inability to carry out fully the complete program, failure to have as much rest as desired, excessive demands on the patient by the family, or lack of cooperation.

The data for the total group (table 2) show clearly the effectiveness of gold therapy and are in keeping with our clinical impression that it is a desirable adjunct as a major component of the complete program necessary to aid in the control of rheumatoid arthritis. These data indicate that more than 300 mg. of gold salts must be given in order to influence the course of the disease favorably.

TABLE 1.—*Response to Therapy of Patients with Mild, Moderate, and Severe Rheumatoid Arthritis, with Comparison of Group Receiving Minimum of 300 Mg. of Gold Salts and Control Group*

	Degree of Rheumatoid Arthritis											
	Mild				Moderate				Severe			
	Gold-Treated		Controls		Gold-Treated		Controls		Gold-Treated		Controls	
Response	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Excellent	8	14	6	7	19	13	10	4	4	2	4	2
		56		31		68		44		49		35
Major	23	42	23	27	79	55	93	40	80	47	83	33
Minor	21	38	47	55	40	28	98	42	69	40	125	55
None	3	5	9	11	4	3	30	13	19	11	38	15
Total	55		85		142		231		172		250	

Evidence of Sensitivity.—Evidence of sensitivity to gold may appear at any time during the course of therapy. A few patients may have manifestations early in the course of the first few injections, and others may not have any until 500 mg. or more has been given. A high percentage of these manifestations are mild, and it is rare that any serious reaction occurs. The sensitivity reactions most commonly seen are glossitis and dermatitis, while albuminuria, gastrointestinal reaction, eosinophilia, colitis, tracheitis, and purpura are less frequent.

TABLE 2.—*Total Group Comparison of Response to Therapy of Patients with Rheumatoid Arthritis, with Comparison of Patients Receiving Minimum of 300 Mg. of Gold Salts and Those Receiving Less*

	Gold-Treated					
	300 Mg. or More		Less Than 300 Mg.		Controls	
Response	No.	%	No	%	No.	%
Excellent	31	8	4	3	20	3
		57		38		38
Major	182	49	48	35	199	35
Minor	130	35	57	41	270	48
None	26	7	29	21	77	11
Total	369		138		566	

Mild albuminuria may occur, but, if it does not increase, the gold salts may be continued. A few nitritoid reactions have been reported. The serious gold reactions, which are rare, are apt to occur when the administration of the gold salts is continued despite the warning appearance of glossitis and dermatitis. When these reactions occur, they usually are controlled by stopping the administration of gold salts. If necessary, antihistamines and oral therapy with steroids are used in treatment for the uncomfortable manifestations. Dimercaprol (BAL)[7] occasionally is necessary for the severely affected. The physician should be on the alert for such manifestations, but, with reasonable supervision, gold therapy can be continued for years without reactions. As many as 50% of patients who have had a mild reaction may be given further gold therapy with use of a smaller dose. Another medical report is in process of preparation to discuss in greater detail evidences of sensitivity.

Summary

Use of gold salts, given by intramuscular route as one component of the program of treatment in rheumatoid arthritis, affords patients 20% better chance of complete recovery or of major improvement. Gold salt therapy may be continued over a period of many years. If evidence of sensitivity occurs, when these manifestations subside further gold therapy may be continued in a majority of patients. Severe reaction to gold occurs in a very small percentage of patients. These symptoms can be controlled with proper treatment.

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AGRANULOCYTOSIS ASSOCIATED WITH THENALIDINE (SANDOSTENE) TARTRATE THERAPY

REPORT OF THREE CASES

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Three cases of agranulocytosis are described. Two patients, aged 81 and 59 years, died. A third, aged 61, recovered despite a fall in white blood cell count to 950 per cubic millimeter, but was severely incapacitated by a cerebral vascular accident at the height of the illness. For reasons here given, it is believed that the drug responsible for the granulocytopenia was thenalidine. The maximum dosage taken by the first two patients was 75 mg. twice a day; the third patient took 75 mg. once a day for 40 days. In each case the thenalidine had been prescribed as an antihistaminic in the treatment of dermatitis or urticaria with pruritus, and after a period of considerable relief from this condition the patient developed fever with soreness of the mouth or throat. The physician who prescribes a potentially hematotoxic drug must be alert to the possibility of agranulocytosis in any patient who complains of sudden fever, chills, or sore throat.

Thenalidine (Sandostene) tartrate [1-methyl-4-N-(2-thenyl) anilinopiperidine tartrate], an antihistamine, was first reported in the European literature in 1953 [1] and in the American literature in 1955.[2] It has now been used in thousands of patients and is reported to be effective in the treatment of various pruritic dermatoses and nondermatological allergic disorders.[3] There has been extensive review of the world literature recently by Gottlieb and Yanoff.[3b]

Serious side-effects, particularly blood dyscrasias, have not been described in any patient.[4] The following cases of agranulocytosis occurring during treatment with thenalidine were recently encountered within a two-month period.

Report of Cases

Case 1.—An 81-year-old female was admitted to the University of California Hospital, Los Angeles, on Dec. 12, 1957, complaining of fever and ulcerations in the mouth of two weeks' duration and urticaria that had occurred intermittently for three and a half months. Fourteen weeks prior to admission (Sept. 3, 1957) the patient saw her private physician because of severe generalized urticaria and indigestion. She was treated with chlorpheniramine (Chlor-Trimeton) maleate tablets during the first week. Concurrently and until Oct. 21 she was given repeated injections of ACTH, and also prednisone, 10-20 mg. per day, intermittently. On Oct. 14, prochlorperazine (Compazine) ethane disulfonate, 20 mg. daily, was prescribed for one week. She received antacids, propantheline (Pro-banthine), 15 mg. four times a day, and Donnatal elixir (a composition of hyoscyamine sulfate, atropine sulfate, hyoscine hydrobromide, and phenobarbital) for two weeks near the end of September.

Ten weeks prior to admission (Oct. 4, 1957) thenalidine tablets, 75 mg. twice a day, were given for two-or-three-day intervals for pruritus. There was some initial improvement, but, because the urticaria recurred, thenalidine in the above dosage was prescribed, daily beginning on Oct. 26, seven weeks before admission. On Nov. 11 the dosage was reduced to one tablet (75 mg.) daily. This was continued until admission.

Other medications included a short course of a sulfonamide for cystitis six months previously, stilbestrol vaginal suppositories, 1 mg. twice weekly for the preceding six months, phenobarbital intermittently for many months, and

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a parenterally administered vitamin-hormone preparation on four occasions during November. On Oct. 23, 1957, a white blood cell count was 9,000 per cubic millimeter, and a red blood cell count 3,690,000 per cubic millimeter. Three weeks after the beginning of thenalidine therapy, the white blood cell count was 7,550 per cubic millimeter, the hemoglobin level 13 Gm. %, and the red blood cell count 3,200,000 per cubic millimeter. An upper gastrointestinal series at the end of September revealed no abnormalities.

Two weeks prior to admission the patient had an abrupt onset of fever (102 F [38.9 C]), weakness, sore throat, headache, and ulcers on the lips and tongue. She was treated with tetracycline-nystatin capsules, pheniramine (Trimeton) syrup, multivitamins, hydrocortisone ointment administered locally to the mouth lesions, and benzathine penicillin G (Bicillin) suspension. There was slight improvement during the next week, but because of the persistence of fever, a slight cough, and a few ulcerative mouth lesions, the patient was referred to the emergency room of the University of California Hospital on Dec. 10. She did not appear seriously ill. The patient's temperature was 101.3 F (38.5 C). Urinalysis was normal, and the white blood cell count was reported as 9,600 per cubic millimeter, but no differential count was done. A chest x-ray revealed signs indicative of a middle-lobe pneumonitis on the right. The patient was sent home with instructions to take tetracycline, 250 mg. four times a day, and aspirin and to apply hydrocortisone ointment locally to the mouth lesions. Two days later she returned complaining of continuing fever with temperatures to 103 F (39.4 C), nausea and vomiting, diarrhea, and recurrence of the urticaria. Chills were denied, and there was no sore throat at this time. However, shortly after admission, she complained of severe dysphagia and sore throat.

Pertinent history included radiation therapy for uterine fibroids 35 years previously. There had been no specific allergies and no urticaria previously. However, there had been frequent episodes of mild nondescript skin eruptions thought to be allergic in nature. On physical examination the patient's blood pressure was 136/88 mm. Hg, her pulse rate 104 beats per minute, and her temperature 102.2 F (39 C). She was an elderly lady in no noticeable acute distress. Her skin was hot and dry, and there was generalized urticaria. There were small superficial ulcers on the legs, tongue, and buccal mucosa, with exudative pharyngitis. A few rales at the base of the right lung were heard. There was slight cardiomegaly, with a soft systolic murmur heard along the left sternal border, and occasional extrasystoles. The liver was enlarged 4 cm. below the right costal margin. Old radiation dermatitis was present over the lower mid-abdomen. The remainder of the physical examination was unremarkable.

Laboratory data on admission revealed a hemoglobin level of 10.9 Gm. %, a packed-cell volume of 34%, and a white blood cell count of 550 per cubic millimeter. Only lymphocytes and a few monocytes were seen on smear of the peripheral blood; platelets were increased. Urinalysis showed albuminuria, acetonuria, and cylindruria. Blood chemistry finding included a blood urea nitrogen level of 22 mg. %; cephalin flocculation of 3+ in 24 hours; a serum protein level of 6.1 Gm. %, an albumin level of 3.0 Gm., a globulin level of 3.1 Gm.; and a nonreactive Veneral Disease Research Laboratories test. On the second hospital day the white blood cell count was 1,000 per cubic millimeter, no granulocytes being seen on the peripheral smear. On the fifth hospital day the white blood cell count had fallen to 425 per cubic millimeter. A sputum culture on admission grew gamma-Streptococcus and beta-Streptococcus, but on the fifth day a throat culture revealed *Pseudomonas aeruginosa*. A blood culture on admission was negative, but others on the fifth and sixth hospital days grew Ps. aeruginosa. A bone marrow aspiration on the fifth hospital day revealed only a few basophilic granulocytes and a small number of atypical myeloblasts and early progranulocytes. Lymphocytes predominated, with a striking increase in megakaryocytes and platelets. The erythroid elements were normal. No leukoagglutinins in the patient's serum to compatible donor white cells with or without the addition of thenalidine could be demonstrated.

In spite of vigorous supportive therapy including multiple antibiotics and hydrocortisone, her course rapidly deteriorated, with death on the sixth hospital day. The gross findings at autopsy revealed severe ulceration of the mucosa of the mouth and esophagus and also of the stomach, small intestine, and colon. The bone marrow appeared soft in the sternum and ribs but firm and red in the vertebrae. Other findings included recent embolization to the pulmonary arteries of both lower lung fields, thrombosis of the pelvic veins, severe coronary artery disease with patchy fibrosis of the myocardium, arterionephrosclerosis, and multiple uterine leiomyomas. The microscopic findings in the bone marrow showed moderate cellularity, with hypoplasia of myeloid elements, patchy increase in fat in the vertebrae, and serous atrophy of the connective tissue elements. Megakaryocytes were increased in numbers. The ulcerations in the gastrointestinal tract extended into the submucosa and were covered with a florid fungus growth resembling *Monilia* with some bacterial growth in addition. There was a moderate surrounding inflammatory reaction with mononuclear cells predominating and only occasional polymorphonuclear leukocytes. The spleen was severly congested, and there was a moderate amount of subcapsular hemosiderin. There was mild fatty change in the liver. Lymph nodes from the neck were hyperplastic and edematous. The findings were considered compatible with the clinical diagnosis of agranulocytosis.

Case 2.—A 59-year-old male was admitted to the University of California Hospital, Los Angeles, on Jan. 29, 1958, complaining of fever and exhaustion of five days' duration. The patient had diabetes mellitus, for two years fairly well controlled with 40 units of protamine zinc insulin daily. Because of findings suggesting diabetic neuropathy, he had received tolazoline (Priscoline) hydrochloride, 25 mg. three times a day, niacin, 50 mg. four times a day, and various vitamin-mineral preparations during this period. A chronic neurodermatitis had been present for the past year. Various local ointments had been prescribed for this, including hydrocortisone cream, diamthazole (Asterol) ointment, and Tashan (pantothenyl alcohol, vitamin A, vitamin D_2, vitamin E) cream. He had taken diphenhydramine (Benadryl) hydrochloride capsules intermittently for a year.

At the end of November, 1957, about 10 weeks before admission, while he was in another city, thenalidine tablets, 75 mg. twice a day, were prescribed, with considerable symptomatic relief from the pruritus. This medication was continued by his private physician and was maintained regularly until the onset of the present illness. Other medication included Alka-Seltzer, Bromo-Seltzer, and aspirin for frequent headaches for several years and antacids and Cholan HMB (dehydrocholic acid, homatropine methylbromide, phenobarbital) tablets intermittently for pyrosis.

Twelve days prior to admission there was an abrupt onset of mild fever, sore throat, and hoarseness. Tetracycline-oleandomycin capsules, one every six hours, were prescribed, with some improvement. However, five days prior to admission his temperature increased to 102.4 F, with extreme exhaustion and headaches, which continued until admission. On the day before admission the patient's white blood cell count was 700 per cubic millimeter, with 92% lymphocytes and 8% basophils in the peripheral smear; his hemoglobin level was 14.8 Gm. %. His blood cell count was known to be normal six months previously. The patient was referred to this hospital one day later with a diagnosis of agranulocytosis.

Physical examination revealed a blood pressure of 140/70 mm. Hg, a pulse rate of 100 beats per minute, and a temperature of 39.5 C (103.1 F). The patient was an obese man, appearing in a toxic condition and weak. His skin was hot and moist. There was an extensive maculopapular erythematous rash over the legs and, to a lesser extent, on the arms. Early diabetic retinopathy was noted. There were several small tender ulcerative lesions in the mouth, and the pharynx was mildly inflamed. The lungs were clear, and a faint systolic heart murmur was heard. The liver and spleen were not felt. A large, tender abscess was present on the left buttock. Deep tendon reflexes were hypoactive, with diminished vibratory and position senses in the lower extremities. The remainder of the physical examination was normal.

Laboratory data showed a white blood cell count of 700 per cubic millimeter, with a predominance of lymphocytes, a few monocytes, and basophilic metamyelocytes. The platelet count was slightly increased; the packed-cell volume was 42%. Urinalysis revealed a trace of sugar and albumin and 2+ acetone. He continued to have moderate glycosuria and acetonuria during the hospital course. His fasting blood sugar level was 326 mg. %. A white blood cell count on Feb. 1 was 750 per cubic millimeter, with no change in the differential count. The erythrocyte sedimentation rate (Wintrobe) was 42 mm. per hour. Culture of the buttock abscess grew Proteus mirabilis, Ps. aeruginosa, Streptococcus faecalis, and Str. zymogenes. Results of a blood culture and bone marrow culture were negative. A chest x-ray and electrocardiogram were not remarkable. A sternal marrow aspiration showed a marked reduction in the number of myeloid cells, with a relative increase in lymphoid and erythroid series. Cells of the myeloid series were rare and predominantly basophils. Megakaryocytes were present in normal numbers.

The patient's course in the hospital was stormy and downhill. Despite therapy with multiple antibiotics, death occurred on the fifth day after admission.

Gross findings at autopsy revealed necrotizing laryngitis and acute tracheitis, a left ischiorectal ulcer, patchy bronchopneumonia, severe pulmonary edema and congestion, and hepatosplenomegaly. The bone marrow was bright red and firm. On microscopic examination it demonstrated hypoplasia of mature myeloid elements, a suggestion of erythroid depression, a normal to increased number of megakaryocytes, and scattered lymphoid follicles. Microscopically, the larynx showed superficial mucosal necrosis, with local congestion, and a mononuclear infiltration in the submucosal area and an absence of polymorphonuclear leukocytes. A less severe but similar reaction was found in the trachea, but some polymorphonuclear leukocytes were noted in the submucosal areas. There was passive congestion, with enlargement of the spleen. Mild fatty infiltration and congestion were evident in the liver, and central homorrhage was observed in a few scattered lymph nodes. The findings were consistent with the clinical impression of agranulocytosis.

Case 3.—A 61-year-old male was seen in consultation at the Culver City Hospital on Feb. 4, 1958, where he had been admitted eight days previously complaining of chills, fever, and a sore mouth. Due to a chronic pruritic atopic dermatitis present for several years, the patient was given thenalidine tablets, 75 mg. daily, beginning on Dec. 19, 1957. This was continued until admission. The only other medication was a multivitamin capsule, Beminal with vitamin C, one daily.

On Jan. 27, 40 days after begining therapy with thenalidine, the patient saw his physician, complaining of fever, chills, a sore mouth, and some diarrhea beginning three days before. His white blood cell count was 2,000 per cubic millimeter, all lymphocytes. He was hospitalized immediatey.

The patient's history was pertinent in that he had had pulmonary tuberculosis from 1941 to 1945, bilateral iritis years ago, and a transitory left hemiparesis in November, 1956. His blood cell count was normal, and a chest film revealed only residual signs of old tuberculosis at that time.

On physical examination the blood pressure was 160/80 mm. Hg, the pulse rate 96 beats per minute, and the temperature 102 F (38.9 C). The patient did not appear acutely ill. The skin was hot and dry, with thickening and excoriations on the arms and face. The pupils were fixed and small. There were early ulcerative mouth lesions, which later became more severe, with a large, deep ulcer in the left anterior tonsillar pillar. The heart and lungs were normal. No hepatosplenomegaly was found. The remainder of the examination was within normal limits.

Laboratory findings included a white blood cell count of 1,350 per cubic millimeter, all lymphocytes; a hemoglobin level of 11 Gm. %; and a red blood cell count of 4,050,000 per cubic millimeter. Urinalysis showed a trace of albumin and 10-15 red blood cells per high-power field and 1-3 white blood cells per high-power field on microscopic examination of the sediment. The Venereal Disease Research Laboratory test was nonreactive. A blood culture on Feb. 5 was negative. A sternal marrow examination five days after admission revealed severe myeloid hypoplasia, only myelocytic and metamyelocytic cells being seen. Megakaryocytes and the erythroid cells were normal. The peripheral white blood cell count fell to 950 per cubic millimeter, all lymphocytes, on the fifth hospital day, but by the ninth day the count was 2,200 per cubic millimeter, with granulocytes being seen for the first time. The differential count revealed 14% band neutrophils, 8% mature neutrophils, 58% lymphocytes, and 20% monocytes. Ten days later the white blood cell count was 11,750 per cubic millimeter, with a normal differential count. Neutrophils showed toxic granulation.

The course in the hospital was marked by initial clinical improvement, but on the sixth hospital day the patient developed a severe right-sided hemiplegia with aphasia. His temperature increased to 103.8 F (39.9 C), which gradually declined to normal by the 18th hospital day. Therapy included multiple antibiotics, ACTH, prednisone, and general supportive measures. The blood picture returned to normal within two weeks after admission, but there was only slight improvement from the cerebral vascular accident at the time of writing.

Comment

The history and findings in three patients with agranulocytosis have been described. Two of these died, but the third recovered. The latter subsequently developed cerebral thrombosis. While it is true that in cases 1 and 2 numerous drugs, including thenalidine, had been given, none of the other drugs listed is known to be associated primarily with agranulocytosis. The time relationships favor thenalidine as the probable cause, but, as in many cases of agranulocytosis, the specific etiological agent cannot be positively identified. In the third case the evidence is more clear-cut, since the patient took only thenalidine and a common multivitamin capsule.

All antihistamines are considered potential offenders in the production of leukopenia or agranulocytosis, but fortunately the incidence of serious reactions is extremely low.[5] Cases of agranulocytosis associated with the administration of antihistamines, methaphenilene (Diatrine)[6] and tripelennamine (Pyribenzamine) hydrochloride[7] have been reported. It is to be noted that it was two years after the latter drug was introduced[8] that the first report of bone-marrow toxicity appeared.[7a] It is of interest that in all these cases the drug had been taken in the recommended dosage range for at least five weeks. This is likewise true in the patients presented in this paper. To our knowledge there are no reports in the literature implicating thenalidine as a possible cause of agranulocytosis. Previous studies have indicated no pathological reactions in the blood picture of any patient, even with prolonged administration, either to the orally given tablets or to the intravenously given combination with calcium gluconogalactogluconate.[9]

It should be unnecessary to emphasize again that the physician must be alert to the presence of granulocytopenia in any patient with sudden fever, chills, or sore throat while that patient is receiving a drug potentially toxic to the hematopoietic system. A white blood cell count and a differential count should be done in any case where there is even a faint suspicion of toxicity. If the results are confirmatory, therapy with the drug must be stopped immediately and appropriate therapy instituted.

Summary

In three cases of agranulocytosis the antihistamine thenalidine (Sandostene) tartrate was administered. Two of the patients died. Agranulocytosis should be considered as the cause of an acute febrile illness when newly introduced drugs or known potentially hematotoxic drugs have been dministered.

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Dr. M. M. Lurie referred case 1, Drs. H. W. Wagensiller and John Reynolds furnished data for case 2, and Drs. M. Jakofsky and W. S. Adams gave permission to report case 3.

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THE *CAROTID PULSE.*—The carotid arterial pulse should be inspected routinely during any clinical examination of the heart. This pulse will help differentiate systole from diastole since it immediately follows the first sound. The causes of an accentuated carotid pulse include aortic insufficiency, aneurysm, hypertensive arteriosclerotic disease, and coarctation of the aorta. A weak carotid pulsation suggests aortic stenosis or a reduced left ventricular ejection (e. g., congestive heart failure). A thrill over the carotid artery is most commonly a transmitted murmur from the aortic or pulmonary valve. A murmur from either valve sets up vibrations in the entire great vessel system, since the walls of the aorta and pulmonary artery are immediately adjacent at the point where the murmurs are produced. There is nothing specific diagnostically about which side of the neck shows the maximum thrill or transmission of a valvular murmur. Carotid artery thrills may also be produced by rapid flow through tortuous, sclerotic vessels or through an enlarged, overactive thyroid gland. Differences in rate between carotid arterial and jugular venous pulses will be noted in atrial flutter or varying degrees of A-V block.—J. R. Blake, M.D., and W. T. Goodale, M.D., Clinical Examination of the Heart, *The Medical Clinics of North America*, September, 1957.

LACK OF SCIENTIFIC VALIDITY OF BODY SURFACE AS BASIS FOR PARENTERAL FLUID DOSAGE

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The customary procedure of using height and weight to calculate the assumed surface area of the body, and then using the result to calculate various metabolic needs of the body, is based on confused logic and inadequate observation. A simple rule of thumb based on weight alone is here shown to be sufficiently accurate, especially since temporary adjustments are dictated by clinical judgment in correcting such conditions as initial dehydration. The rule for infants less than one year of age calls for 60 ± 15 ml. of water per pound (132 ± 33 ml. per kilogram); for children from 1 to 5 years, 50 ± 15 ml. per pound (110 ± 33 ml. per kilogram); for children above 5 years, approximately 40 ± 15 ml. per pound (88 ± 33 ml. per kilogram).

It is the purpose of this paper to (1) evaluate the scientific validity of methods for determining surface areas; (2) challenge the validity of body surface (even if it could be accurately determined) as the basis for relating body metabolism and other physiological functions; and (3) present a simple rule of thumb based on weight alone for estimating normal body fluid requirements for pediatric patients which we will show gives the same results as those determined by more complex systems. In essence, the rule of thumb consists of the following formulas: (*a*) infants less than one year of age, 60±15 ml. of fluid per pound; (*b*) children from 1 to 5 years, 50±15 ml. of fluid per pound; and (*c*) children above 5 years, approximately 40±15 ml. per pound.

Many recent publications discussing fluid therapy[1] have presented systems for computing fluids and electrolyte needs on the basis of calculated surface area. The resultant methods have been complex and require the use of nomograms, logarithms, or equations. It is our belief that these complex systems, though superficially impressive, are not based on a sound scientific foundation. It is our intent to show that calculation of normal fluid requirements can be met by the use of much simpler rules with greater scientific validity, although the end-results are similar.

Appraisal of Surface Area Concept

The consideration that fluid requirements may be directly correlated with the body surface of the individual has been presented in several publications.[1] Historically, this concept of the correlation of metabolism (and, by inference, intake requirements) to surface area was first emphasized by Rubner in 1883. Many subsequent publications have explored this premise, both in human subjects and in animals, with varying interpretation of the results, some agreeing and others disagreeing with Rubner's hypothesis.

Acceptance of a direct correlation of surface area to fluid needs implies also acceptance of the following premises: (1) a reasonable accuracy of calculation of surface area from equations (or nomograms) utilizing the weight and height of the subject; (2) the acceptance of body surface as a unit of physiological function; and (3) the consistent relationship of the magnitude of metabolism to surface area regardless of the age, health, and other potentially influencing factors.

Validity of Estimation of Surface Area.—Since direct measurement of the surface area of an ill or even a well patient is obviously impractical, there are in general usage standard charts[2] or, more frequently, nomograms[3] from which the surface area can be approximated with use of the height and weight of the subject. Although the nomograms for this purpose are simple to employ, the accuracy of the approximated surface area obtained cannot be more precise than the original measurements upon which they were formulated. Furthermore, such methods should be universally applicable to subjects, from the smallest viable premature infant to the largest obese adult.

Since the first estimate of surface area by Abernathy in 1793, many workers have measured the surface area of subjects of varying ages by different methods, usually in small numbers, and have attempted to derive formulas for calculating surface area from these data. Despite the voluminous literature on this subject, it is well to note that the total number of subjects of all ages upon which direct surface measurements have been made by any of several methods (coating technique, surface integrator devices, and triangulation technique) are 406,[4] and, of these, 254 measurements were on chil-

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observations and by an even greater abundance of different interpretations. Advocates of the theory of the physiological significance of surface area[8] have indicated such a correlation in the results of the extensive metabolic studies of Benedict. However, Benedict[9] stated in his own conclusions from his investigations, "It is believed that far greater progress will be made by discarding all thoughts of a uniformity in heat loss and emphasizing the nonuniformity in heat production." This conclusion and the relevant discussion preceding this interpretation would hardly seem to support the principle of a constant relation of either heat loss or heat production to surface area among differing individuals or different species. More recent studies of both dog and human subjects[10] afford further confirmations of Benedict's conclusion. Furthermore, Kleiber notes that metabolism relates more consistently to weight than surface area.

The correlation of other physiological functions to surface area has been reported.[7] One particular area perhaps deserves special comment: interpretations of renal clearances are consistently reported in terms of calculated surface area of the subject. Homer Smith, in his discussion of the basis for this standard, concludes that kidney weight is preferable as a unit for comparison, but that, in view of the wide range of kidney weight from those calculated, the preferable unit at present is surface area. It would appear then that even in the field of renal physiology a standard of surface area may not be a completely closed subject. Recent investigations of heart volume, total body hemoglobin and blood volume, cardiac output, plasma volume, blood pressure, glomerular filtration rate and effective renal plasma flow, total body water space, and extracellular and intracellular water space seem to demonstrate an equal or better correlation of these physiological functions with weight than with calculated surface area.

These studies suggest that surface area is only another manner of indicating the size of a subject. Logical support for weight as a reference point is found in the concept that the magnitude of physiological activity depends upon the active protoplasmic mass which has been designated "lean body mass." The active metabolic weight is derived from measured weight minus the metabolically inactive component (primarily adipose tissue). Studies of metabolism in human subjects in tropical zones by Galvao[10] demonstrate that basal metabolism is proportional to weight, the relationship decreasing with fatter subjects. Surface area proved inapplicable as an indication of anticipated metabolism.

Evidence for Consistent Relationship of Metabolism to Surface Area.—It is of more than historical interest that Rubner originally (1883) stated that approximately 1,000 calories represented the heat production per square meter of surface area of warm-blooded animals (dogs). In his last publication (1931) he noted that the average metabolic level of mammals at 30 C (86 F) was about 615 calories per meter. In spite of Rubner's correction, the "magic number" of 1,000 calories per unit of surface area persists. The significance of 1,000 calories per square meter of surface is not in the quantity of calories chosen but in the concept that the heat production per unit of surface area is uniform regardless of age, size, or species. To explore this concept Benedict[9] and later Brody and Kleiber reviewed their own data plus those available in the literature. The latter arrived at the conclusion that the unit of surface area could not be fitted to observed energy metabolism of different animals and that weight was the most suitable unit for metabolism. This finding has subsequently been confirmed by Hemmingsen (1950) and Schelling (1954). Benedict[9] had earlier stated that "the surface area concept does not apply within the species and that it most certainly does not apply between species." This is demonstrated in his chart (fig. 1) comparing observed average heat production of each animal species corrected to a standard unit of one square meter of surface area. The curved line, as noted in the original text, was drawn in by inspection, but if a consistent relationship existed for these varying species when referred to a unit of surface area then a nearly horizontal line would have been expected.

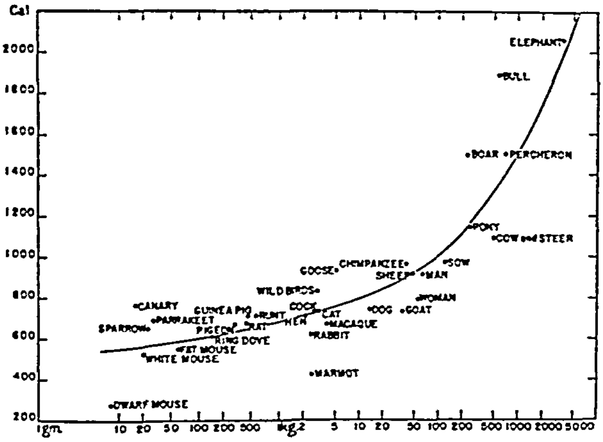


Fig. 1.—Semilogarithmic chart showing trend of average heat production per square meter of surface area of each animal species referred to average body weight. Weight range from 8 Gm. to 3,700 kg. Reproduced with permission of publisher.[9]

Benedict and Talbot[11] determined surface area by the original linear formula of DuBois and DuBois[5a] (which involves measuring the length and breadth of each part of the body and multiplying by a constant) on normal infants and children. The resulting data give a more accurate determination of surface area than estimation by nomograms. Basal metabolic rates were then determined under carefully controlled conditions. This tec
should theoretically reveal most exactly the

ship of surface area to heat production since it satisfies as closely as practical the use of exact surface area values for comparison to metabolism in children.

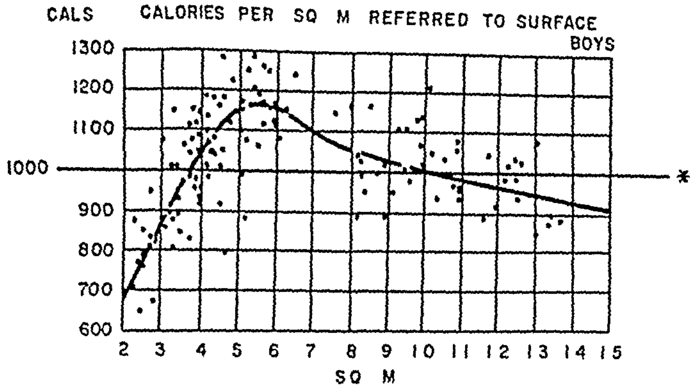


Fig. 2.—Basal heat production of boys per square meter of body surface per 24 hours referred to surface. Reproduced with permission of publisher.[11] * = anticipated basal heat production per square meter of surface for all ages when derived from concept of constant heat production per unit of body surface.

They then compared measured basal heat production to measured surface area as determined by the original DuBois' technique[5a] (fig. 2). The heat production of each subject was corrected to one square meter of surface area and then plotted against the total surface of the individual. By such plotting the existence of a direct relationship of surface area to heat production would be manifested by a straight line. However, Benedict and Talbot note that such a straight line relationship does not exist. Instead, there is a progressive increase of heat production up to about 0.5 square meter of body surface (a finding also shown by Murlin and Hoobler in their metabolism studies in 1915) and thereafter a decrease with larger subjects. They further observed that a line corresponding to 1,000 calories per square meter will be exceeded by ± 25 to 30% in a large number of subjects. Data comparing metabolism to weight resulted in a relationship very similar to that found for metabolism-surface area correlations.

The above observations make difficult the acceptance of relating metabolism directly to surface area. It is evident that total metabolism increases with size of the individual but is not consistently increased with surface area. Furthermore, neither can weight alone systematically describe this increase of heat production. The ideal unit for comparing metabolism in one animal to another has not been ascertained but may ultimately be approached through consideration of the "active metabolic protoplasm," or "lean body mass." This concept has certainly not been developed for clinical use. Other units must presently be utilized, with cognizance of their limitation.

Simple Method Based on Weight for Estimating Maintenance Fluids for Infants and Children

Although the use of weight for estimating fluid needs has been less frequently emphasized in recent years, it has continued to occupy a prominent position in current publications.[12] The use of such systems has not been proved invalid; in fact, recent observations relating various physiological functions to weight substantiate the continued use of the patient's weight as a reliable gauge for estimation of fluid requirements.

A modified[12] scale for calculating fluid dosage by a rule of thumb based on weight is represented in figure 3. The mean approximates the figures suggested in the literature. After the addition of a ± 15 ml. of fluid per pound range (selected on the basis of common clinical experience), a diagonally oriented cone-shaped figure is obtained, signifying the broader limits of tolerance for the larger (and older) patients. This figure then represents the mean and upper and lower ranges for maintenance fluids for pediatric patients, and is summarized in

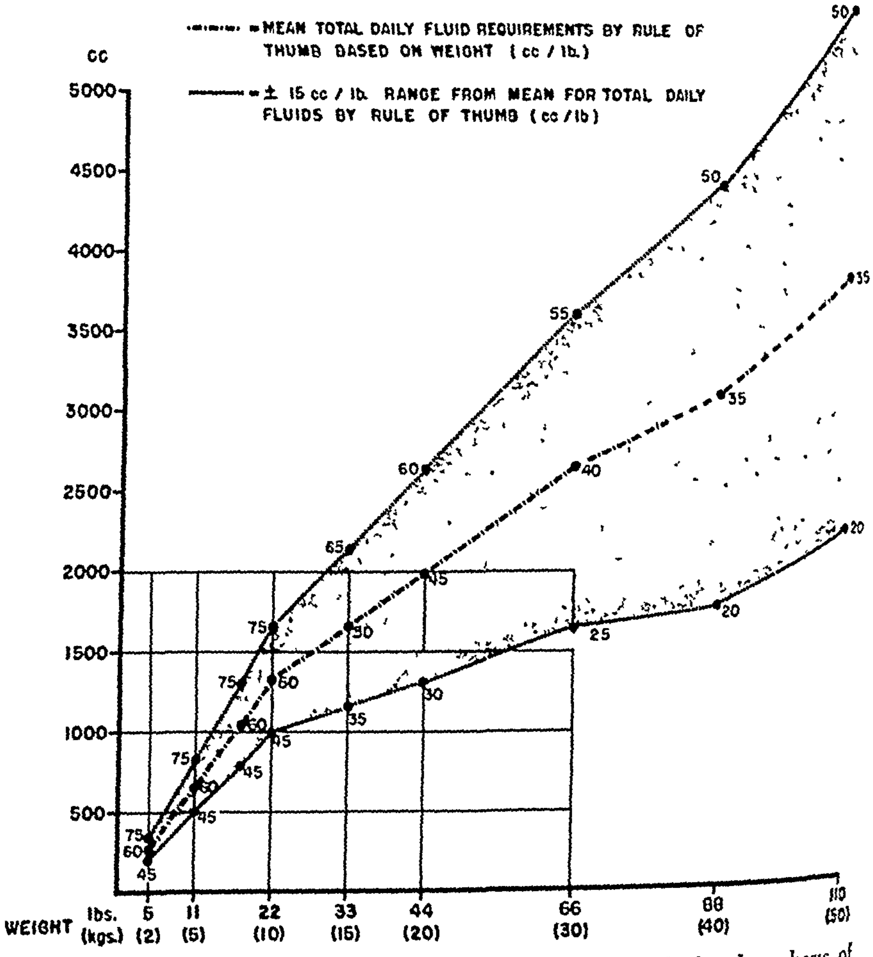


Fig. 3.—Daily fluid needs for infants and children, calculated on basis of weight.

table 2 In figure 4, maximal tolerance and minimal requirements of fluids by surface area calculations are presented.

In order to compare fluid requirements determined by these two systems, superimposition of the two graphs has been made (fig. 5). The composite chart shows similar patterns for maximal and minimal fluid needs. Thus, regardless of any other point of discussion, there seems to be little need for nomograms or surface area calculations since the final results are the same when simply weight alone is used for calculation.

A point of discrepancy, however, between the two systems is in the larger quantities of fluid for maintenance allotted by the rule of thumb method to children weighing between 11 and 33 lb. (5 to 15 kg.). As pointed out by Holliday and Segar[17] and illustrated in figure 2, the metabolism (and relative fluid needs) of the growing child is greatest between the ages of 6 to 24 months, corresponding to the weight range of 11 to 33 lb. Inasmuch as the surface area calculations assume a constant metabolism per unit of surface area, regardless of age or other factors, this well-documented observation of a heightened metabolism at this period of life has thus been neglected.

Comparisons of Surface Area, Weight, and Caloric Expenditure for Calculating Fluids

Although it is the principal intent of this communication to explore the physiological basis for determining fluid dosage by surface area, certain recent publications[17] relating fluid requirements to energy expenditure should not be excluded from this discussion. The basis for these latter systems is the observation that fluid and electrolyte requirements are proportional to the caloric expenditure of the patient. The caloric expenditure is derived from tables relating weight to basal metabolic rate plus increments for physical activity, fever, specific dynamic activity, and growth. Several methods incorporate the estimated increments into the final equations, while some suggest percentage increases above basal expenditure expected for each of the above factors. The background and derived methods are sound and we do not infer otherwise. However, for practicing physicians who daily encounter feeding-formula calculations with volume of formula determined in ounces per pound (or milliliter per kilogram) a similar method of determining parenteral fluid needs would seem appropriate. As shown above, the calculations by the simpler rule of thumb (weight) method give essentially the same results as those obtained by other systems.

Table 2 —*Daily Fluid Requirements of Infants and Children*

Age, Yr	Mean Oz Lb	 Ml /Lb	Range
Under 1	2	60	± ½ oz (15 ml)/lb from mean
1 5	1⅔	50	
5-8	1½	45	
8-11 . .	1⅓	40	
11 14	1¼	35	

Further comparisons have been made of the surface area and weight rules against that derived from calculation of caloric expenditure (Holliday and Segar[17]). The caloric expenditure values are represented by the dotted line superimposed in figures 4 and 6. These values approximate more closely the minimal fluid needs by weight than by surface area criteria. Calculations show the greatest difference between the weight method and the caloric expenditure system is only 13%, as compared to a difference of 50% between surface area and caloric expenditure method. These comparisons would seem to further substantiate the validity of the rules of thumb method based on weight.

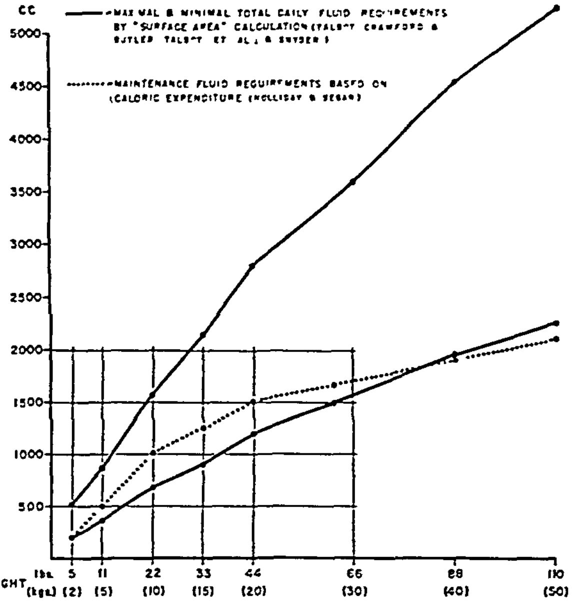
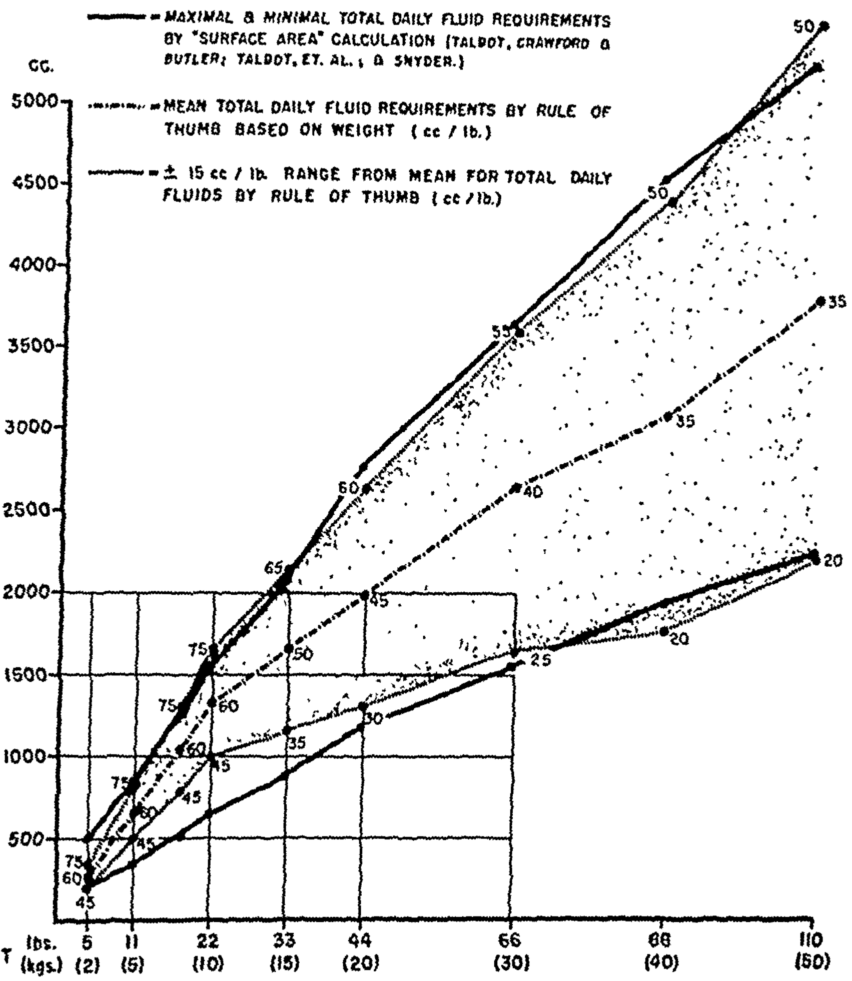


Fig 4 —Daily fluid needs, calculated on basis of caloric expenditure versus surface area

Another significant point is that physicians using surface area or caloric expenditure for calculating fluids often return to weight for correction of dehydration. Talbot and associates[16] point out that, since "hypovolemia is a phenomenon related to mass, total dose is estimated as 3 to 5% of body weight," and Darrow (1954) has defined the losses of both fluids and electrolytes subsequent to dehydration as calculated per kilogram. Such observations would seem to present support for a sensible and versatile method of estimating fluid dosage utilizing simply the weight of the patient.

Further Check Points for Parenteral Fluid Program

Correction of Dehydration.—It should again be emphasized that our simple rule of thumb is for maintenance fluids, and is not intended to prescribe the necessary amount for a dehydrated patient. Correction of dehydration is best calculated on the basis of weight, and 90 ml. of fluid per pound (or 3 oz. per pound) per 24 hours is usually an adequate volume with which to begin rehydration. Evaluation of the patient from the aspect of previous losses and continuing deficits is necessary. Extenuating circumstances such as persistent hyperpyrexia or renal disease with polyuria may dictate administration of even larger daily amounts of fluid, and only by reappraisal can physicians continue to prescribe correctly in such situations. The use of daily weights and the clinical appearance, including skin turgor and the frequency and volume of urination, all contribute valuable information regarding the state of hydration. In other words, no set of rules for parenteral administration of fluids in sick babies can substitute for clinical judgment.



ig. 5.—Daily fluid requirements of infants and children, calculated on basis veight versus surface area.

fter correction of the initial dehydration, which es seldom less than two days and frequently es longer, a value for total daily fluids approxitely midway between the mean and minimal amounts would be a reasonable volume to employ for maintenance, with use of doses nearer the mean value for infants and young children, although more is usually recommended.

Quality and Types of Solution for Parenteral Fluid Therapy.—Although this communication is directed toward the volume aspect of parenteral fluid therapy, the quality or types of solution cannot be totally ignored here. Butler and Talbot (194 recommend that the young infant receive 125 of isotonic sodium chloride solution for maint nance; the older infant, roughly 250 ml.; and t child, 350 ml. per day. The remaining volume woul consist of 5 or 10% dextrose in water. Isotoni sodium chloride solution up to one-third of the tot daily fluids is frequently recommended; our ow clinical experience has repeatedly shown that in th presence of normal renal function such quantities o electrolyte are frequently needed and well tolerate In the presence of acute dehydration, in whic instance the majority of the loss has been sustaine by extracellular compartment, initially up to one half of the infusing solution may consist of isotonic sodium chloride solution with reduction o this proportion after adequate circulation has bee reestablished. The exception is particularly displayed by the infant with hypertonic dehydration for whom during initial rehydration, only one-fourth to one-third of the total daily solution should be electrolyte solution.

Parenterally given potassium is seldom indicated for patients for whom resumption of orally given fluids is anticipated within one or two days. For longer periods of parenteral administration of fluid or in certain disease states, potassium salts in the form of potassium chloride, using a dose of 1 to 1.5 mEq. per pound per day, may be safely given intravenously so long as renal function is adequate. The use of polyionic solutions (i. e., multiple electrolyte composition) in place of mixtures of isotonic sodium chloride solution and 5 or 10% dextrose as outlined above may be employed with the rule of thumb based on weight.

The continued use of the clinical appearance of the patient, his daily weight and daily urine volume, as well as selected blood chemical determinations, are further and necessary check points for any parenteral fluid program.

Comment

A review of the literature pertaining to surface area may be summarized as follows: 1. Surface area cannot be accurately estimated by use of the methods most frequently employed in clinical medicine. 2. The various physiological functions do not have a consistent correlation to surface area. Surface area has not been substantiated as the ideal unit for interpreting physiological data. 3. In no warm-blooded animal does the magnitude of metabolism parallel his surface area.

Instead, the data available show that, with growth and increasing mass of an organism, there must be an accompanying increase in weight, metabolism, cardiac output, renal function, and other activities as well as in surface area. Thus, surface area and metabolism increase with size, although not consistently parallel, and not as a result of metabolism's dependence on surface area, but because both reflect increasing magnitude (size) of the organism. Current literature thus substantiates a conclusion reached 43 years ago by Benedict and Talbot (1914):[14]

> If, therefore, it is maintained that the total metabolism is proportional to the body-surface, it should be stated that this is not due to the fact that there is a loss of heat from the body-surface and that Newton's law on cooling determines the intensity of the metabolism, but that with normal individuals the body-surface, blood-volume, the area of the trachae and the aorta, and probably the active mass of protoplasmic tissue, are all in simple mathematical relation to the body weight. Thus the apparent relationship which has previously been observed between the heat-output and the body-surface with normal or nearly normal individuals has an explanation in that with such individuals a simple relation exists between the body-surface, blood-volume, body-weight, and the mass of active protoplasmic tissue.

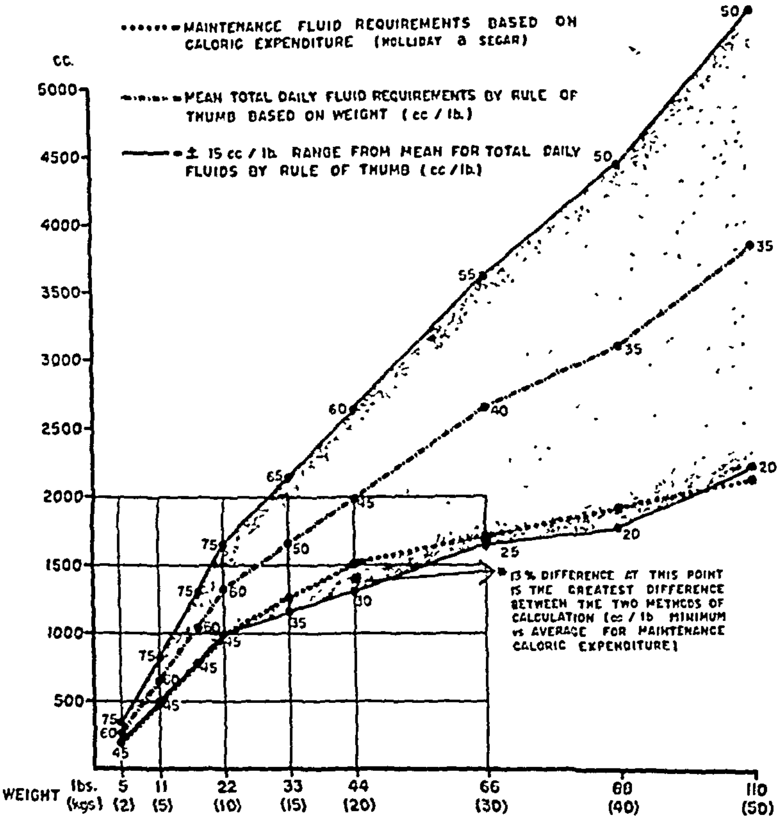


Fig. 6.—Daily fluid needs for infants and children, calculated on basis of weight versus caloric expenditure.

No rule for calculating fluids obviates the necessity for careful evaluation of each patient. It is realistic to reiterate that there are marked variations of contributing circumstances, both recognized and unknown, present from one patient to the next. No concise rule for estimating fluid dosage shall exist as long as patients differ from one another.

Conclusions

No method for calculating body surface is accurate enough to make it superior to weight as a unit for calculating fluid requirements. If body surface could be accurately measured there is little evidence that it would be superior to weight as a unit for comparing physiological functions. A simple rule of thumb based on weight alone gives substantially the same results for determining dosage of maintenance fluids as a more complicated system in general use in which estimates of body surface are derived from nomograms.

1313 E. Ann St. (Dr. Wilson).

A more extensive bibliography is available upon request to authors.

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ENDOCARDITIS DUE TO COAGULASE-POSITIVE STAPHYLOCOCCUS PYOGENES VAR. AUREUS

REPORT OF EIGHTEEN CASES AND REVIEW OF ADDITIONAL NINE AT THE LOS ANGELES COUNTY HOSPITAL, 1947-1956

Herbert Shubin, M.D., David C. Levinson, M.D.
and
George C. Griffith, M.D., Los Angeles

In 27 cases of endocarditis due to coagulase-positive Staphylococcus aureus, the mortality rate was 74%. The diversity of presenting symptoms and physical findings often gave little clue to the underlying illness. Failure to suspect the diagnosis early in the course of the disease may well have contributed to the high rate of mortality. The choice of the antibiotic which is most likely to prove effective is difficult to make early in the course of the disease, in view of the variable resistance of the staphylococci to antibiotics. It is recommended that a combination of antibiotics be given at the onset. The frequent repetition of blood cultures and sensitivity studies during the course of illness is of prime importance.

Despite antibiotics, endocarditis due to coagulase-positive Staphylococcus pyogenes var. aureus remains a major therapeutic problem. The mortality rate has been 74% in 27 adults with this type of endocarditis treated at the Los Angeles County Hospital from 1947 through 1956. In nine cases in the period from 1947 through 1949 reported by Levinson and co-workers,[1] the mortality was 67%. In 18 subsequent patients treated from 1950 through 1956, the mortality rate has been 78%.

The purpose of this paper is to review the clinical features, course, therapy, and autopsy findings in the 18 cases occurring from 1950 through 1956 in an attempt to delineate a more effective program of management for the future.

Clinical Data—General Findings

Age and Sex.—Eleven of the 18 cases occurred in patients 50 years of age or younger, 7 in patients over 50. Thus, 39% of the patients were over 50 years of age. Of the "over-50" group, three patients were in the sixth decade, three in the seventh decade, and one in the eighth decade. The number of men and women was equal.

Antecedent Heart Disease.—Valvular heart disease was present in 11 of the 18 patients prior to infection with Staph. aureus. Of these, six had involvement of the mitral valve alone, three involvement of the aortic valve alone, and two involvement of both aortic and mitral valves. In one patient with aortic insufficiency and stenosis, the serologic test for syphilis was positive; however, in the presence of aortic stenosis, the etiology probably was not syphilitic. No postmortem examination was obtained in this case.

Nature of Precipitating Infections.—The nature of the precipitating infections is summarized in table 1. In no instance in this series was the infection introduced through parenteral self-administration of narcotic drugs—a frequent source of infection according to other investigators.[2] In one case, infection followed curettage after an incomplete spontaneous abortion. No other postsurgical cases were found

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in this series. We would like to draw attention to the absence of infections after prostatic surgery, a relatively common etiological factor in other reported series.

Symptoms.—Early in the course of the disease, marked malaise was common. Chills occurred in 42% of the cases, and cough in 33%. Other symptoms were referrable to the precipitating infection, as noted in table 1.

Duration of Illness Before Therapy.—In the four patients who survived, the average duration of illness before therapy was five days (range, three to seven days). In these patients, therapy was started on the first hospital day, after one or more samples of blood had been drawn for culture.

In 14 cases with fatal outcome, the illness preceded therapy for periods varying from two days to several weeks. Of this group, the duration of illness before therapy was 1 to 4 days in five patients, 5 to 10 days in two, 11 days or more in four, and not determined in three. Of this last group of three patients, one had an acute exacerbation of chronic ulcerative colitis, another had hemorrhagic pancreatitis with subsequent infection, and the third had hemangiomatosis (Rendu-Osler-Weber's disease), with no clear-cut time noted as to the start of the infection.

Clinical Data—Physical and Laboratory Findings

Physical Findings.—Physical findings will be discussed under the general headings of heart murmurs, pulmonary, abdominal, skin, and neurological findings, and miscellaneous.

TABLE 1.—*Precipitating Infection in Endocarditis due to Coagulase-Positive Staphylococcus Pyogenes var. Aureus*

Precipitating Infection	Cases, No.	Duration of Illness Before Hospital Admission
Upper respiratory infection	6	2 to 16 days
Pyelonephritis	2	{2 wk., acute {several mo., chronic
Acute hemorrhagic pancreatitis	1	6 wk.
Ulcerative colitis	1	2 wk., acute
Hemangiomatosis	1	Undetermined
Infected arteriovenous aneurysm of foot	1	Undetermined
Dilation and curettage (for spontaneous incomplete abortion)	1	3 days
Tubal infection	1	4 days
Pustular skin rash due to coagulase positive Staph. aureus	1	4 wk.
Undetermined	3	Undetermined

Heart Murmurs: Heart murmurs were present in 12 of the 18 patients at the time of admission to the hospital. In one case, the patient had been examined previously on a number of occasions as an outpatient, but no murmur had been detected. In three of the six patients without a heart murmur at the time of admission, a murmur appeared during the course of the illness. In only one patient in whom a heart murmur was heard initially was the murmur observed to change in quality and intensity during the illness. In 3 of the 18 patients, no heart murmur was heard at any time during the illness, but evidence of valvular involvement was found at autopsy.

Pulmonary Findings: Four patients with tricuspid valve involvement had physical findings indicative of pulmonary disease. In three of the four there was autopsy or x-ray evidence of multiple pulmonary infarcts or abscesses. In the fourth, autopsy examination disclosed bilateral pneumonia.

TABLE 2.—*Staphylococcus Pyogenes var. Aureus Sensitivity to Six Antibiotics, by In Vitro Concentration per Milliliter, in Fifteen Patients**

No. of Case†	Chloramphenicol, 30 Mcg.	Erythromycin, 15 Mcg.	Bacitracin, 20 Units	Tetracyclines, 30 Mcg.	Streptomycin, 100 Mcg.	Penicillin, 10 Units
1	S	S	S	R	R	R
2	...	...	...	...	...	S
3	S	...	S	S	S	S
4	S	...	R	S	S	S
5	S	S	S	S	S	R
6	S	S	R	R	S	R
7	S	R	S	R	R	R
8	S	R	S	R	R	R
9	S			S	S	S
10		...			R	R
11	S	S	S	R	R	R
12	R	...	...	S	S	R
13	S	S	...	S	R	S
14	S	S	...	S	R	R
15	S	S	S	R	R	R
No. sensitive	12	7	7	7	7	5
No. studied	13	9	9	13	14	15

* Disk method employed for determining bacterial sensitivity: R = resistant, S = sensitive.

† Patients in cases 1-3 survived, and patients in cases 4-15 died.

Abdominal Findings: At no time was splenomegaly observed. The liver was enlarged in four instances.

Skin Findings: In only 2 of the 18 patients did petechiae, not present at time of hospitalization, develop during the course of the illness. One of the 18 patients had splinter hemorrhages. Osler's nodes were present in another. Clubbing was not noted in any case.

Neurological Findings: Nuchal rigidity was present in two cases. Coma occurred in two other patients and convulsions in one.

Miscellaneous: Joint inflammation was not a feature of this series, although Dowling and coworkers,[3] in a review of the literature in 1952, noted an incidence of joint inflammation of 33%. Our series differed from those reported on earlier, also, in that multiple subcutaneous abscesses were not found in early stages of the disease.

Laboratory Findings.—In reference to laboratory data, findings in these areas will be discussed: blood cultures and sensitivity determinations, blood and urine examinations, and electrocardiography.

Blood Cultures and Sensitivity Determinations: In all cases at least two or more blood cultures of Staph. aureus coagulase–positive bacteria were obtained. In 11 of the 18 cases, a positive blood culture was obtained on the first hospital day, in two cases on the second hospital day, and in an additional two cases on the fourth hospital day. In these 15 cases, the positive culture was obtained from the initial blood sample which was cultured. In view of the difficulty in establishing an early diagnosis of this disease, the finding of positive cultures on the initial blood sample is most significant.

Bacterial sensitivity studies are shown in table 2. The disk method was employed for determining bacterial sensitivity, except in a few instances in which the tube dilution method was used for the determination of penicillin sensitivity.

Blood and Urine Examinations: Thirteen of the 18 patients had hemoglobin levels of 12 Gm. per 100 cc. or less at the time of hospital entry. In this anemic group, the average hemoglobin value was 10.5 Gm. As a rule, the anemia progressed slowly with the illness. In three instances the bacterial endocarditis apparently was solely responsible for hemoglobin levels of 9 Gm. per 100 cc. or less. On admission, the average white blood cell count was 15,000 per cubic millimeter—with a range of 6,000 to 28,000. Polymorphonuclear cells averaged 83%.

Albuminuria was present in 11 of the 17 cases in which urinalyses were done. Aside from that found in two patients with pyelonephritis, hematuria was not characteristic of the early part of the disease. Generally, urinalyses were done infrequently after hospital admission, for this reason: it is difficult to evaluate subsequent hematuria.

Electrocardiography: Four of the 18 patients had atrial fibrillation, as shown on the electrocardiogram. In all of these patients mitral stenosis was present. In the four patients with tricuspid valve involvement, the rhythm was of sinus origin; however, the tricuspid valve involvement was of relatively short duration, having developed with the final illness. Also noteworthy was the presence of sinus rhythm in two patients who subsequently proved to have abscesses of the myocardium.

Therapy and Course of Disease

Selection of Therapy.—Most of the patients were started on therapy with penicillin given intramuscularly in doses ranging from 300,000 to 1,200,000 units per day. After identification of the microorganism and determination of sensitivities, penicillin was given either in much larger doses than initially or was withdrawn. Usually only at this time, after identification of the Staph. aureus, were other antibiotics added or substituted.

In the patients with fatal illness the average dose of penicillin was 12 million units per day. The average daily dose of other antibiotics was as follows: chloramphenicol (Chloromycetin), 2.5 Gm.; erythromycin, 1.5 Gm.; streptomycin, 1.0 Gm.; tetracyclines, 2.0 Gm.; and bacitracin, 75,000 units given intramuscularly. Many patients received two, or even three, of these antibiotics, but combinations of two or more were rarely given early in the course of the illness. Despite these dosages, 14 of 18 patients did not respond to treatment.

In some cases with fatal outcome, the doses of antibiotics were considerably higher: one patient received 45 million units of penicillin intravenously per day for 21 days, to no avail.

Course of Disease.—The average daily temperature range was between 101 and 104 F. (38.3 to 40 C), with increasing sepsis. One patient with mitral valve involvement had an embolus to the right arm in the second week of illness, and another patient with tricuspid valve involvement had a pulmonary embolus in the third week of illness. Two of the four patients with tricuspid valve involvement developed failure of the right side of the heart six weeks after the onset of the illness. Five of the 14 patients with valvular lesion of the left side of the heart developed pulmonary edema at intervals ranging from two weeks to several months after the illness began. In one patient progressive uremia occurred, and in two additional patients terminal bleeding episodes were noted. Two patients lapsed into coma within one day after hospital entry.

Outcome and Autopsy Findings

Outcome of Disease.—Of the 18 patients, only 4 survived and 14 died. The survival rate was 27% in persons 50 years of age or under and only 14% in persons above the age of 50. Four of the 14 fatalities occurred during the first four days of hospitalization, despite the fact that therapy was begun the first day of hospitalization. In these four instances, the short course of therapy may not have been sufficient for proper evaluation. Of the other 10 patients who died, 6 received treatment for at least one week and 4 for at least three weeks.

Therapy for the four patients who survived was comparable to that received by the patients who died. All of the patients who survived received penicillin. One, with a Staph. aureus sensitivity to 0.7 units of penicillin per milliliter, survived on a penicillin dosage of only 2,400,000 units per day given intramuscularly for four weeks without other antibiotics. A second survivor had a microorganism sensitive to penicillin (10 units per milliliter) and to streptomycin and dihydrostreptomycin. This patient responded favorably to penicillin, 10 million units per day administered intramuscularly, with 0.5 Gm. of streptomycin and 0.5 Gm. of dihydrostreptomycin given intramuscularly, all for five weeks. In a third survivor the Staph. aureus was not sensitive to penicillin but was sensitive to erythromycin and chloramphenicol. This patient received erythromycin, 1.6 Gm. per day, and chloramphenicol, 1.0 Gm. per day, both for three weeks. Streptomycin, 2.0 Gm. per day, and penicillin, 20 million units per day given intravenously, and four weeks, also were administered. In the fourth survivor Staph. aureus was also cultured, but no record of the sensitivity studies was found. This patient received penicillin, 4 million units per day, intramuscularly, for four weeks.

Autopsy Findings.—Autopsies were performed in 10 of the 14 cases with fatal outcome. The findings in the heart were as follows: the mitral valve was the site of vegetations in eight of 10 cases, the aortic valve in three, and the tricuspid valve in three. In all three instances in which the tricuspid valve was involved, the patients had no known valvular disease at the onset of the fatal illness. In none of the patients with tricuspid vegetation was there a history of parenterally injected narcotics. In one case with no previously known valvular disease, vegetations occurred on both tricuspid and mitral valves. In three cases without previously known valvular disease, vegetations were found on the mitral valve in the absence of any vegetations in the right side of the heart.

Abscesses were a notable feature of the disease. In the 10 patients in whom autopsy was done, the organs most frequently involved were brain (6), kidney (5), spleen (4), heart muscle (2), and lungs (2). Splenic enlargement was not noted clinically in any patient, although splenic abscesses were found in four.

Comment

Of this present series of 27 cases of endocarditis due to coagulase-positive Staph. aureus, the mortality rate was 74%. This figure may be compared with that reported by Wilson and Hamburger,[4] who surveyed 35 cases of endocarditis due to Staph. aureus and Staph. albus and found a mortality rate of 87% for patients treated before 1948 and a mortality rate of 60% for patients treated between 1948 and 1954.

Failure to suspect the diagnosis early in the course of the disease may well have contributed to this high rate of mortality. In over 50% of the cases with fatal outcome, the illness was present for more than one week before hospitalization was effected and before blood cultures were taken. Frequently, several days more elapsed before sensitivity studies directed therapy to the proper antimicrobial agent.

The great diversity of presenting symptoms and physical findings often gave little clue to the underlying illness. The difficulty in suspecting the diagnosis was illustrated by the absence of a heart murmur at the time of hospital admission, in one-third of the patients. In these cases early definitive diagnosis was possible only with a blood culture, although the toxic picture in some was suggestive of a septicemia.

Among the two-thirds of patients who did show heart murmur there was often a significant delay intensity [illegible] hospitalizing these patients. Once the patient was hospitalized, blood cultures were taken early and treatment started—usually with penicillin. However, because the organism was sensitive to penicillin (10 units per milliliter) in only 33% of the cases, a further delay in effective therapy was introduced.

The choice of the antibiotic which is most likely to prove effective is difficult to make early in the course of the disease, in view of the variable resistance of the staphylococci to antibiotics. Development of strains resistant to penicillin has been pointed out by Rammelkamp and Maxon,[5] Rantz and Kirby,[6] and Schnitzer and Grunberg.[7] Wise and co-workers[8] have emphasized the increased resistance of staphylococci to other antibiotics, which has appeared with their increased usage.

The selection of antibiotics before sensitivity studies have been completed must depend, therefore, on information as to which antibiotics have proved most effective—both locally and currently—against Staph. aureus. It is recommended that a combination of antibiotics be given at the outset. This is advisable on two grounds: the possible potentiation of effect,[9] and the delay in producing resistance.[10] Once there is a suspicion that endocarditis is present, blood should be drawn immediately for culture and for sensitivity studies and vigorous therapy launched at once with at least two antibiotics which, both locally and currently, are most likely to be effective.

With bacterial endocarditis due to other organisms, where the progression of the disease may not be so rapid, a schedule of doubling and redoubling the antibiotic dosage, in the face of inadequate response, has been used with some success. This approach appears to be completely inadequate for the eradication of staphylococcic endocarditis. In view of the 74% mortality rate attendant on this disease, it is our firm opinion that large doses of at least two antibiotics should be used from the very beginning of therapy after initial blood cultures have been done. Because staphylococci are currently frequently resistant to penicillin and streptomycin, it often may be advisable to use other antimicrobial agents initially.

The frequent repetition of blood cultures and sensitivity studies during the course of the illness is of prime importance. Changing antibiotic sensitivity may indicate the value of additional antibiotics, which may be added to or substituted for those already in use.

Although staphylococcic resistance to antibiotics has been increasing, in no instance in the present series was an organism found which was not sensitive to at least two of the antibiotics commonly employed today. Although this may not always continue to be the case, the great pitfall has been the delay in initiating vigorous therapy with properly selected antibiotics sufficiently early in the disease.

Summary

The mortality rate of 74% in 27 cases of endocarditis due to coagulase-positive Staphylococcus pyogenes var. aureus in adults treated at the Los Angeles County Hospital in the past 10 years emphasizes the highly fatal course of this disease. The difficulty in early diagnosis is pointed up by the fact that one-third of the 18 cases treated from 1950 through 1956 occurred in patients with no known preceding valvular disease.

The value of blood cultures in early diagnosis is reflected in the finding of a positive culture from the initial blood sample in 15 of these 18 cases. Delay in early therapy was a significant factor in the fatal outcome in over half of them. Initiation of therapy with antibiotics to which the staphylococci subsequently proved to be insensitive was a contributing factor to the high mortality rate in additional cases. At least two antibiotics to which the staphylococci—both locally and currently—are most sensitive must be selected. Drawing of blood samples for culture and sensitivity determinations and immediate initiation of vigorous therapy on suspicion of septicemia is mandatory for an improved survival rate.

1200 N. State St. (33) (Dr. Griffith).

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DIRECT MATCHING OF BLOOD FOR TRANSFUSION.—It is impossible for the blood bank laboratory to examine all patients and all donors for all the known factors; in practice, only the ABO group and the Rh (D) type is determined. Emphasis is placed upon a direct compatibility test to screen out the instances, admittedly uncommon, in which an unusual antibody is present, specificity determination being a time-consuming subsequent procedure. The use of unmatched blood raises always the possibility of reaction due to the presence of an unsuspected antibody, above all in patients previously transfused or previously pregnant. . . . Any hospital liable to face urgent or emergency cases should deem it an obligation to provide adequate facilities on the premises for matching blood at any hour of the day or night. This comment would be superfluous were it not that, even now, there are hospitals which lack such facilities. . . . Transfusion is of common application in many clinical fields and it is of major significance as regards the life of the patient. Decision and action is often in the hands of recent graduates. For these reasons it is suggested that somewhat more attention be paid in medical schools to blood transfusion and related topics. The most conservative as regards transfusion are those who have witnessed severe or fatal reactions in one or more of their patients. Adding to such blatant examples the possibilities of hepatitis some three months later, of haemolytic disease of the newborn months or years afterwards and of haemolytic reactions with any future transfusions, all this should be sufficient to counsel caution. And there are particular dangers with unmatched blood. There is no such thing as "Universal Donor" blood.—Cecil Harris, B.Sc., M.D., F.R.C.P., "Universal Donor" Blood or the Persistence of a Myth, *Medical Services Journal*, April, 1958.

HOSPITAL LAUNDRY AND REFUSE CHUTES AS SOURCE OF STAPHYLOCOCCIC CROSS-INFECTION

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and
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The modern, multistoried hospital is provided with chutes for the disposal of soiled laundry and of waste. The part played by such chutes in the dissemination of air-borne bacteria was investigated. Air movement within the chutes and at their openings was studied by methods which included the use of yellow-smoke candles and fluorescent powder; bacteria were cultured and phage-typed. Especially above the ninth floor, there tended to be an upward movement of air in the chutes, with small volumes leaking out constantly from cracks around the doors and large volumes flowing out into the corridors when chute doors were opened. The opening of a chute door when material was dropped from above permitted strong gusts of contaminated air to blow out into the corridor. The majority of chute staphylococci studied were resistant to penicillin, and their phage-patterns were those typical of bacteria causing hospital cross-infections. The chutes present an undeniable hazard that demands correction. Until better ones can be designed, it will be necessary to change the procedure for handling both soiled laundry and other materials. The practice of putting materials from infected patients directly into waste-chutes must be discontinued, and the bedclothing of patients with even mild staphylococcic infection should be handled like that of patients in isolation.

During a study on neonatal staphylococcic infection, it seemed desirable to compare the phage patterns of strains in the nursery with those circulating among adult patients in the hospital at large. Since patients with a staphylococcic infection may readily contaminate their linen, the air, and subsequently the hospital dust, it was thought that the air exhausted from the laundry and refuse chutes might provide a representative and easily sampled pool of the patients' staphylococci.

It was soon found that the exhaust air contained considerable numbers of coagulase-positive penicillin-resistant staphylococci. Further inspection of the chutes revealed them to have a persistent strong updraft capable of returning these staphylococci to the hospital corridors whenever the chute doors were opened. Observations of the chutes as a potential source of staphylococcic infection are described here.

Physical Plan of the Hospital

Floor Utilization.—The Herbert C. Moffitt Hospital is a modern inpatient teaching hospital, completed in 1955, with a capacity of 470 beds and 40 bassinets. Floor utilization is as follows: basement, chute receiving rooms and central supply; floor 1, administration; 2, kitchen and dining rooms; 3, radiology; 4, surgery and recovery room; 5, diagnostic laboratories; 6, pediatrics; 7, neurology and neurological surgery; 8, ophthalmology, otorhinolaryngology, and orthopedic surgery; 9, surgery and urology; 10, medicine and surgery; 11, medicine; 12, cancer research; 13, research laboratories under construction; 14, gynecology; 15, obstetrics and nursery; and 16, air-circulating installations.

The plan of all floors, except the first through the fifth, is illustrated in figure 1. The nursery occupies the east wing and the delivery room the west wing of the 15th floor—each separated from the remainder of the floor by swinging doors. The surgical theatres are located on the south wing of the fourth floor. This floor and the obstetric floor are air-conditioned; other floors are mechanically ventilated by forced air circulation.

All floors are served by a laundry chute and a refuse chute—each 2 ft. in diameter. Centrally located openings are provided on each floor near the nurses station and not far from the service elevators, which are used to transport patients (fig. 1 and 2). The dumb-waiter used to convey sterile supplies is adjacent to the refuse chute. The refuse chute takes all rubbish, including dressings wet with blood, serum, or pus. Placentas were also put down the chute when the hospital first opened, but this practice was discontinued because of resulting mechanical obstruction. Soiled gowns, linens, and blankets of all patients, except those on isolation orders, are put down the laundry chute. (Patients with postoperative wound infections, draining abscesses, and eczema are often not isolated.) Linen of patients on isolation is placed in a double cloth laundry bag before being put down the chute.

From the Department of Microbiology, School of Dentistry and School of Medicine, (Dr. Hurst); the Department of Pediatrics, School of Medicine (Dr. Grossman), University of California Medical Center; and the Division of Occupational Health, Cowell Memorial Hospital of the University of California (Mr. Ingram and Mr. Lowe).

Characteristics of Chute Air-Flow.—Ventilation of the chutes is by natural air-convection, with exhaust outlets located on the roof. Normal air movement is upward but is subject to wide fluctuations in flow—including total reversals—due to pressures imposed by the building ventilation system, atmospheric conditions, and the passage of materials down the chutes.

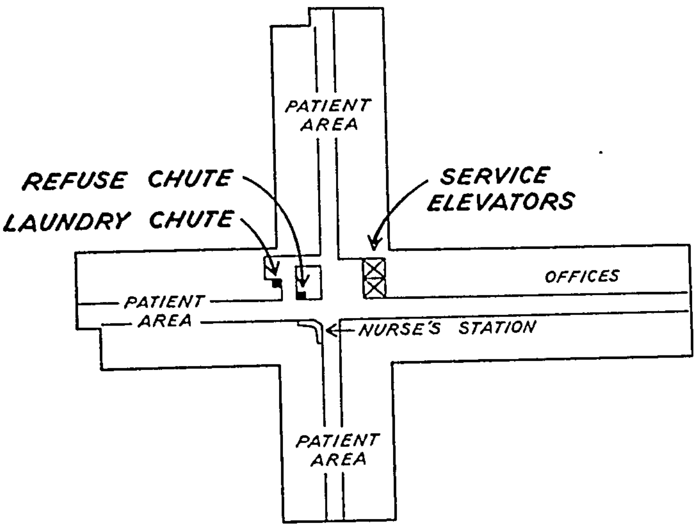

Fig. 1.—Typical floor plan of Herbert C. Moffitt Hospital.

Typical quantification of air movement within the chutes and at their openings when no material is passing down is shown in table 1. Normally, both chutes are strongly negative relative to the chute receiving rooms in the basement. Pressure differentials on the fifth to ninth floors are not so pronounced as those above and below, and air movement to and from the chutes on these floors is essentially tidal.

Table 1.—*Air Flow Measurements, in Feet per Minute, Within and at Openings of Chutes when No Material is Passing Down**

	15th Floor		10th Floor		4th Floor	
Time of Day	At Opening	Within Chute	At Opening	Within Chute	At Opening	Within Chute
(Laundry chute)†						
8:30 a.m.	+300	85	+300	80	—200	50
9:30 a.m.	+330	110	+150	80	—200	75
10:30 a.m.	+220	60	+ 70	50	—170	100
1:30 p.m.	+250	130	+140	60	—110	80
2:30 p.m.	+260	60	+ 90	45	—110	80
(Rubbish chute)‡						
8:30 a.m.	+300	35	—200	40	—270	45
9:30 a.m.	+220	100	— 70	40	—330	80
10:30 a.m.	+360	30	—280	60	— 90	90
1:30 p.m.	+400	20	+210	..	—210	...
2:30 p.m.	+230	30	+270	40	—220	180

* Plus signs indicate airflow from chute into adjoining hospital area. Minus signs indicate airflow in opposite direction. Chute velocities are all upward.

† Effective opening is 12 by 17 in. (1 42 sq. ft.).

‡ Effective opening is 6 by 18 in. (0.75 sq. ft.).

Laundry chute doors are open for 5 to 10 seconds per loading so that during a typical use of this chute on the 15th floor some 30 to 60 cu. ft. of air is released into the corridor. Each use of the refuse chute results in a similar but smaller influx. Corresponding increments in decreasing amounts enter the building corridors during loading on all upper floors down to, and including, the 10th. In addition, there is constant leakage of 1 to 5 cu. ft. per minute through the cracks around the closed chute doors on these floors.

Intermittently, large gusts of air are forced into the corridor areas on all floors and into the basement receiving rooms when the chute doors chance to be open at the time of passage of laundry or rubbish. These gusts have been found to reach velocities as high as 1,800 ft. per minute. Leakage from cracks around the chute doors is also greatly increased by the pressure induced each time material is dumped from above.

In order to obtain pictorial evidence of the flow of air from the chutes and along the corridors, tests were made with yellow-smoke candles. Smoke was released in the laundry chute at the 13th floor and was observed as it emerged on the 15th floor. Figure 3 shows the effluence at the 15th floor four to six minutes after release.

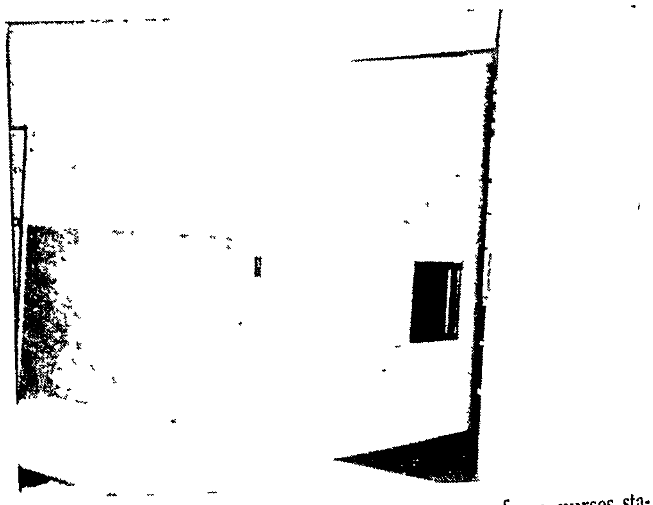

Fig. 2.—Laundry chute opening as seen from nurses station.

Chute dispersal of small light particles, comparable to bacteria-laden dust and lint, was investigated with zinc-8-hydroxyquinoline, a nontoxic powder of 1 to 5 μ individual particle size with a characteristic fluorescence under ultraviolet light. No comparable fluorescent material was obtained in a 200-liter sample of the 15th-floor air passed through a black Millipore filter (fig. 4), nor was any found upon inspection of the 15th-floor linoleum with ultraviolet light.

Approximately one tablespoon of the fluorescent powder was atomized into the chute at the 14th floor level; simultaneously, the 15th floor chute door was held open the width normally used for soiled linen disposal. The air and linoleum of the 15th floor were then examined for the fluorescent powder. In less than one minute large quantities of powder had poured out of the open 15th floor chute door. In 15 minutes time the linoleum within a 25-ft. radius of the chute was liberally sprinkled with the powder. Within 40 minutes appreciable quantities were recovered in a 400-liter air sample collected by the Millipore filter at the nursery door 20 ft. away (fig. 4). Small quantities were found on the nursery floor soon after the closed door to he nursery was opened, and larger quantities were apidly brought in on the shoes of nurses entering rom the contaminated area.

An hour after the experiment, fluorescent powder was detected in small quantities outside the laundry chute door of the sixth floor. Inspection of the chute vestibules on all floors 12 hours later revealed easily detectable quantities, indicating distribution of the powder throughout the chute. Some of it was caked on the chute walls and probably had been carried down by wet laundry articles. The otal observations left little doubt that small light particles placed in the chute could be spread readily throughout the hospital.

Bacteriological Observations

Methods.—In the preliminary study the refuse-chute air was sampled twice daily by inverting an agar plate over the roof exhaust for a period of several hours. Laundry chute contamination was determined by sampling the lint caked under the hood protecting the roof exhaust.

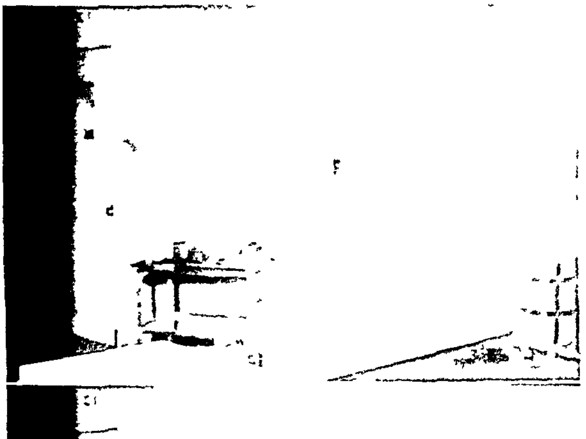

Fig. 3.—Test smoke emerging from door of 15th-floor laundry chute held ajar by bundle of soiled linen. *Top,* four minutes after smoke was put in at 13th floor. *Bottom,* six minutes later.

To obtain more quantitative counts, volumetric samples were taken within and in front of the chutes with an impinger-bubbler.[1] One-hour samples were collected at a rate of 10 liters per minute between 9:30 and 10:30 a. m. on the 13th floor level. Because this floor was still under construction, it did not house patients or hospital personnel and was ventilated entirely by outside air from unpaned windows. No coagulase-positive staphylococci were found in the air of this floor before the sampling of the chute interiors; those later collected just outside the chute doors therefore represented those released when the chute doors were opened.

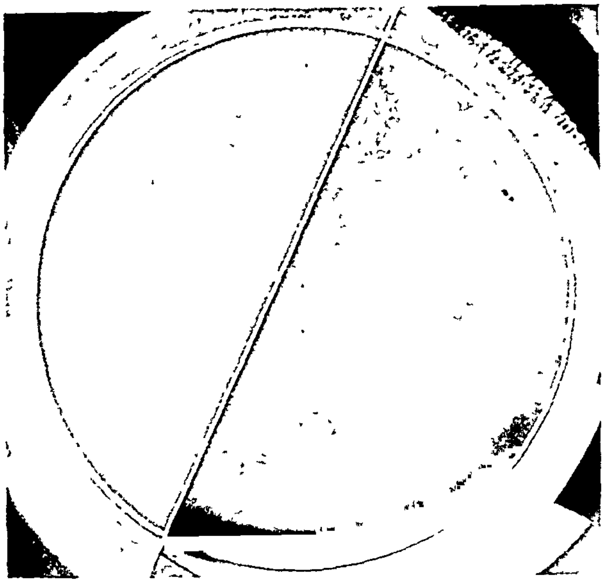

Fig. 4.—Millipore aerosol filter photographed under ultraviolet light after sampling 15th floor air before (*left*) and after (*right*) fluorescent powder was put in laundry chute.

Tellurite-glycine agar, modified to contain 0.0025% potassium tellurite, was used to cultivate coagulase-positive staphylococci from all samples collected. On the surface of this medium, coagulase-producing staphylococci form large black, bluish, or gray colonies after 48 hours incubation, while many coagulase-negative staphylococci and most other bacteria are inhibited. Coagulase production was confirmed by the slide-coagulase test. The data pertain only to coagulase-positive staphylococci.

Phage typing was done according to the method of Williams and Rippon.[2] The typing set included phages 3A, 3B, 3C, 6, 7, 29, 39, 42B, 42D, 42E, 47, 52, 52A, 53, 54, 55, 70, 71, 73, 75, 77, 79, 80, 81, 523, 971, and VA$_4$. Sensitivity to penicillin, as well as to other antibiotics, was determined by disks containing the highest Difco concentration.

Laundry Chute.—Lint collected on three days was found to contain 1.0×10^6, 3.5×10^6, and 0.4×10^6 staphylococci per gram, respectively, indicating that the chute air contained particles comparable to hospital floor dust in degree of contamination. Hutchison and Bowman[3] obtained 1×10^4 to 1.5×10^5 staphylococci per gram of dust collected in a nursery where staphylococcic infections were a frequent occurrence among the newborn infants.

Volumetric samples of the air within the laundry chute contained 635 staphylococci per cubic foot on Aug. 21, 275 on Aug. 23, and 440 on Aug. 29, representing a contamination level more than double that which occurs during the dressing of infected burns and several hundredfold higher than that observed in hospital wards, nurseries, and surgical theaters (table 2). The samples collected just outside the chute door contained 125 staphylococci per cubic foot on Aug. 21, 15 on Aug. 23, and 95 on Aug. 29, indicating that as much as one-fifth of the chute contamination may return to the corridor when the door is open only 1 in.

TABLE 2.—*Coagulase-positive Staphylococci Recovered in Volumetric Air Samples*

Reference	Colonies/ Cu. Ft.	Source
Rountree & Barbour[9]	1.0-5.0	Hospital nursery
	0.0-0.1	General hospital wards
Wallace & Duguid[10]	0.01-0.04	Hospital nurseries
	0.02-0.10	Maternity wards
Lowbury[11]	130	Dressing station for burns
Hardyment and others[12]	1.0-7.0	Hospital nursery
Wysham and others[13]	0.45	General nursery activity
	0.87	Changing bedding of infant carriers
	0.08	Obstetrics floors
	2.14	Wards of adult patients with staphylococcic infections

Refuse Chute.—Daily counts obtained from plates placed over the refuse chute exhaust are shown in table 3. The higher morning count probably reflects the greater activity in refuse disposal which occurs during this time. The all-day average (1.7) is more than twice the average count (0.7) obtained from plates exposed on the patient floors between July 24 and Aug. 28 and is comparable to that reported by Clarke and others,[4] who obtained a maximum of 1.6 colonies per plate per hour in surgical wards where staphylococci cross-infections were frequent.

TABLE 3.—*Plate Samples of Exhaust from Refuse Chute*

	Exposure, Hr.		Colonies/Plate/Hr.	
Date	a.m.	p.m.	a.m.	p.m.
June 20	3.00	4.00	1.00	0.80
21	3.75	3.75	0.80	0.90
24	5.00	3.00	4.00	0.00
25	3.00	4.75	0.70	0.80
26	3.50	4.00	10.00	0.50
27	3.50	4.00	1.70	2.50
28	2.75	4.50	0.70	1.10
July 1	2.50	3.00	2.40	3.70
2	3.25	5.00	2.80	1.60
3	5.50	2.50	0.00	0.40
5	3.00	3.00	1.30	1.30
8	2.50	4.50	0.40	0.40
Av.	3.44	3.83	2.20	1.20

The refuse chute counts are additionally significant when it is noted that each colony represents a Staphylococus-bearing particle sufficiently light to have traveled two or more floors to the hospital roof. On Aug. 22, 27, 28, and 30, volumetric samples of the refuse chute air contained 55, 110, 35, and 1 staphylococci per cubic foot, respectively, while samples collected just outside the chute contained 1, 0, 5, and 0 per cubic foot.

Phage Types and Penicillin Sensitivity.—Seventeen colonies obtained from the laundry chute lint samples and 73 colonies obtained from the refuse chute exhaust were selected at random for phage typing. Although any one sample from either source usually contained a variety of phage types, a single type sometimes predominated. The two chutes yielded 17 different phage types in addition to untypable strains. The great majority were penicillin-resistant strains having group III phage patterns (table 4 and 5), which are most frequently encountered in hospital infections.

TABLE 4.—*Bacteriophage Patterns of Staphylococci Cultivated from Lint from Laundry Chute*

Strain No.	Phage Group	Phage at Routine Test Dilution	Undiluted Phage	Sensitivity‡	Colonies, No.
1	III	(54)/(VA_4)*	47/54/75/VA_4/971	R	12
2	III	7/47/53w†/54/75/VA_4/971	...	R	1
3	III	6/7/42Bw/42Ew/47/53/54/75/VA_4/971	...	§	1
4	III	70/VA_4w	...	§	1
...	Untypable	Not lysed	Not lysed	§	2

* Reaction sometimes absent.
† w indicates weak lyses.
‡ R indicates penicillin-resistant.
§ Sensitivity not tested.

Two of the strains were of particular interest because they were also isolated from the infections of patients hospitalized during the spring and summer months. Strain 1, which predominated in both the lint and the refuse exhaust samples, was isolated from 10 patients, of whom 7 undoubtedly acquired it during their hospital stay (table 6). Disk sensitivity tests indicated the strain to be sensitive to chloramphenicol but resistant to the tetracyclines, erythromycin, streptomycin, and penicillin.

Strain 17, which was detected in the refuse exhaust on three separate days, was responsible for an outbreak of neonatal impetigo and maternal mastitis between January and mid-March and was cultured from the infections of seven patients on other services—six of whom undoubtedly acquired their infection in the hospital (table 7). This strain has been found to be sensitive usually to chloramphenicol and erythromycin but resistant to the tetracyclines, streptomycin, and penicillin. The phage pattern and antibiotic sensitivity of this strain indicate a strong similarity to the strain which has caused infections in many other hospitals.[5]

Comment

After a decade of antibiotic therapy, hospital cross-infections still remain a major medical problem due to over-reliance on the antibiotics, antibiotic resistance developed by staphylococci, and careless disregard of the aseptic principles propounded by Semmelweis and Lister.

Possible vectors for the spread of resistant staphylococci are numerous, and their relative importance is not entirely clear. The recent demonstration that group A streptococci do not seem to be infective after they have resided in the environment for any length of time[6] has led some clinicians to believe that the aerial route plays a minor role in all hospital infection. It remains to be proved, however, that staphylococci undergo a similar loss of infectivity in the environment. Those who discount the aerial route of staphylococcic transmission generally believe that these infections result from intimate contacts with the secretions of infected persons—either directly or indirectly.

It will be difficult to assess the full significance of our observations on dispersal of resistant staphylococci by the hospital chutes until the relative importance of the various transmission pathways can be clarified. Few will deny that such dispersal is undesirable; many will agree with us that it is alarming. Since the chutes which have been described are of accepted design, their characteristic drafts probably prevail in many other multistoried hospitals.

Each time the laundry and refuse chute doors are opened on the 10th to 15th floor, large volumes of contaminated air flow out into the corridor, and smaller volumes constantly leak out from cracks around the doors. The opening of a chute door while material is being dropped from above may permit an air gust of a velocity up to 1,800 ft. per minute to enter the corridor. Such air may contain *200 to 600 staphylococci per cubic foot and may* bear lint carrying several million staphylococci per gram. Many of these staphylococci may have been deposited in the chutes very recently, for smoke and fluorescent powder put into the laundry chute returned almost instantaneously to the corridor after traveling up one or more floors.

The majority of chute staphylococci which were examined in detail were resistant to penicillin and often to other commonly used antibiotics. Their

TABLE 5.—*Bacteriophage Patterns of Staphylococci Cultivated from Refuse Chute*

Strain No	Phage Group	Phage at Routine Test Dilution	Undiluted Phage	Sensitivity‡	Colonies, No
1	III	(54)/(VA$_4$)*	47/54/75/VA$_4$/971	R	40
2	III	7/47/53w†/54 75 VA$_4$ 971	..	R	10
5	III	47/54/971	...	R	4
6	III	7/42B/42E/47/53 54 75/VA$_4$/971	...	R	8
7	III	7w/47/54	..	R	1
8	III	42Bw/42E/47w/54 73w/971	.	S	1
9	III	7w/42B/42Ew/70 73w 81w/VA$_4$	...	R	1
10	III	75	.	R	1
11	III	No lysis	VA$_4$/971	R	2
12	III	No lysis	6/54/VA$_4$/971	R	1
13	III	No lysis	7w/42E/54/70w/ 73w/75w/971	S	1
14	III	No lysis	77	S	1
15	III	No lysis	75w/971	§	1
16	II	3A/3B/3C/39/55w 971	...	S	1
17	I-III	52w/42B/80/81	..	R	3
.	Untypable	Not lysed	Not lysed	S	2

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* Reaction sometimes absent

† w indicates weak lysis

‡ R indicates penicillin resistant, S penicillin sensitive

§ Sensitivity not tested

TABLE 6.—*Cases in Which Strain 1 Staphylococcus Was Isolated*

Case No	Date Cultured	Days Hospitalization After Infection	Culture Source	History
Definitely hospital acquired				
1	5/18	47	Abdominal wound	Serious abdominal wound infection after Bricker procedure; reoperation required
2	5/28	8(died)	Chest wound	Pyothorax after surgery for aortic aneurysm
3	6/2	49	Abdominal wound	Severe abdominal wound infection with septicemia after two operations; thromboendarterectomy and cholecystectomy
4	7/4	24(died)	Thoracotomy	Pyothorax after resection of cancer of lung followed by thoracoplasty because of bronchopleural fistula
5	8/9, 8/13, 8/16	60	Abdominal wound	Multiple abdominal abscesses after exploration for obstructive jaundice
6	8/9	51	Abdominal wound	Severe abdominal wound infection after gastroduodenostosis with splenectomy
7	8/13	10	Pus	Wound infection after excision of fibrosarcoma
Possibly hospital acquired				
8	5/23	6	Colostomy	Drainage of abscess around old colostomy site
9	5/31	23	Blood culture	Admitted with reticuloendotheliosis with complicating
10	8/9	11	Abdominal wound	Abscess around colostomy opening staphylococcic pneumonia

TABLE 7.—*Cases in Which Strain 17 Staphylococcus Was Isolated*

Case No	Date Cultured	Days Hospitalization After Infection	Culture Source	History
Hospital acquired				
11	2/18, 2/21	154	Wound abscess	Septicemia, pericarditis with multiple staphylococcic abscesses following initial valvulotomy
12	6/1	7(died)	Thoracostomy fluid	Staphyloccic pneumonia following pneumonectomy
13	6/18	45	Rectal pus	Wound abscess, rectal abscess, pulmonary infection, and peritonitis in patient operated on for perforated peptic ulcer
14	6/30	14	Wound	Wound infection following Bricker procedure
15	8/15	28	Subcutaneous abscess	Multiple furunculosis and subcutaneous abscess developing during prolonged hospitalization for shortness of breath on exertion and penicillin therapy
16	9/2	30	Ear swab	Abscess of parotid gland in debilitated patient hospitalized for another illness
17	6/18, 6/19, 7/8	77	Pus	Osteomyelitis of skull after bur hole

phage patterns were those which are frequently associated with hospital cross-infections (group III). Some phage patterns were similar to those of staphylococci isolated from patients who were hospitalized at the time of the investigation, and bedclothing and dressings from these patients undoubtedly contributed to the contamination of the chute. Chute staphylococci may well have been responsible for some of the infections which were hospital-acquired.

The staphylococci which emanate from the chutes would not necessarily have to travel as far as the patients' rooms in order to produce infection. The chutes are only 25 ft. from the service elevators used to transport patients to and from surgery and the diagnostic services, and they are immediately adjacent to the dumb-waiter carrying surgical supplies and dressing kits. A strong gust from one of the chutes could heavily contaminate the outer wrappings of the "sterile" surgical supplies or the bedding and garments of a patient just returning from surgery.

The chutes present an undeniable hazard which demands correction. Hospital refuse and laundry chutes should be designed to prevent the return of any chute air to the hospital. Better chute construction will require considerable engineering skill and may prove both difficult and expensive. More judicious consideration of the materials which are thrown into the chutes will help to reduce chute contamination. Routine autoclaving of all disposable infected materials before discarding them would seem obviously mandatory, but it is not usually done in this hospital and was only recently revived in another hospital.[5e] While bedclothing of patients with even mild staphylococcic infection should be handled like that of patients in isolation, this is not always being done.

Review of our hospital chute construction and usage leads us to agree with others [7] that failure to appreciate and apply aseptic principles is contributory to the staphylococcic cross-infections which now occur in many hospitals. ". . . neglect to use the truth like the one found by Semmelweis makes (us) wonder whether it's more science we need or more thorough and honest use of what's already known." [8]

Summary

Movement and staphylococcic contamination of air of the laundry and refuse chutes in a modern 16-story hospital have been investigated. The airflow studies revealed that there was considerable movement of air from the chutes into the hospital corridors. This movement was strongest on the upper floors and released as much as 30 to 60 cu. ft. of air in the 5 to 10 seconds a chute door was opened for normal use. All floors were subject to large gusts if the doors were open during the passage of materials down the chute.

The air of the laundry chute was found to contain 200 to 600 staphylococci per cubic foot and that of the refuse chute up to 100 staphylococci per cubic foot. The lint in the laundry chute was also heavily contaminated by staphylococci. The majority of these staphylococci were found to be penicillin-resistant and had group III phage patterns.

Many of the bacteriophage patterns were similar to those of staphylococci isolated from infected patients hospitalized at the time of the investigation. It is probable that these staphylococci were deposited in the chutes by contaminated bedclothing and by discarded infected refuse (surgical dressings, swabs, etc.). Many of the patients had acquired their infection in the hospital, and it is possible that the chutes may have contributed to the spread of the infective staphylococci.

It is recommended that (1) hospital chutes be designed to prevent the return of contaminated particles to hospital corridors and patient areas and (2) the practice of putting materials from infected patients directly into the chutes be discontinued.

Third and Parnassus Avenues (22) (Dr. Grossman).

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CLINICAL IMPLICATIONS OF POSTOPERATIVE TRANSIENT ALDOSTERONISM

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The ratio of sodium to potassium excreted in the urine was observed in five patients before and after surgical operations of various degrees of severity. After operation the ratio invariably fell, but it returned to normal in the course of a few days. Simultaneous assays of the urine for aldosterone showed that the excretion of this hormone was increased several fold during the first and second postoperative days. This transient postoperative aldosteronism is thus inversely related to the sodium retention and directly related to the potassium excretion. These facts point to the existence of an intricate regulatory mechanism for maintaining the balance of electrolytes after surgery and indicate the need for care in the postoperative use of saline solution.

Although the acute and marked changes in sodium and potassium metabolism which take place after any operation of a medium degree of severity have been widely recognized,[1] the mechanism, or mechanisms, responsible for their occurrence remains obscure. Many theories which have been postulated lack a solid experimental basis. A few years ago it was suggested that the adrenal cortex might play a major role, but the evidence, in general, was not more convincing than for the other theories. This paucity of definite data probably stemmed from difficulties in the estimation of adrenocortical hormones and from the lack of precise knowledge on the nature of the genuine electrolyte-regulating corticoid.

Four years ago an adrenocortical hormone having a remarkable activity in promoting sodium retention and potassium excretion was isolated and named aldosterone.[2] This discovery gave new impetus to the study of conditions associated with electrolyte disturbances. The aim of this paper is to point out the clinical implications, obvious and probable, derived from some studies made on the excretion of aldosterone in patients undergoing surgical operations.

Experimental Studies

By a rather complex method of bioassay in the adrenalectomized rat,[3] the changes in aldosterone content in 24-hour collections of urine were studied preoperatively and postoperatively in several patients. Sodium and potassium concentrations were also estimated by flame photometry in the same urine specimens. In order to generalize the results obtained, the patients studied comprised adults of both sexes, suffering from a variety of clinical conditions, who were subjected to operations of various degrees of severity and who showed no evidence of electrolyte imbalance or endocrinological disturbance prior to operation. The results are summarized in figure 1.

Changes in Sodium and Potassium.—In the upper scale of this graph the changes in the sodium/potassium ratio before and after operation have been represented. The use of the urinary sodium/potassium ratio has the advantage that it summarizes in a single figure the fluctuations in

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opposite directions of two variables. It is also the most sensitive and accurate index[4] of aldosterone activity. The striped column *represents the* preoperative value which has been arbitrarily assumed to be 100. All other values are expressed as a percentage of this value for each patient. Since it has been shown[5] that there is a significant correlation between the urinary levels of aldosterone and the logarithm of the sodium/potassium ratio, the logarithms of the percentage figures have been plotted instead of the actual values. The two solid columns represent the values for the first and second days after operation. The dotted column represents one value selected from the late postoperative period. The criterion utilized to include in the graph the latter value was to choose that of the first postoperative urine collection which was shown to have a sodium/potassium ratio approximately equal to the preoperative value.

It may be easily seen (fig. 1) that in the early postoperative period there is a considerable reduction of the sodium/potassium ratio, which returns to the preoperative value in the late postoperative period.

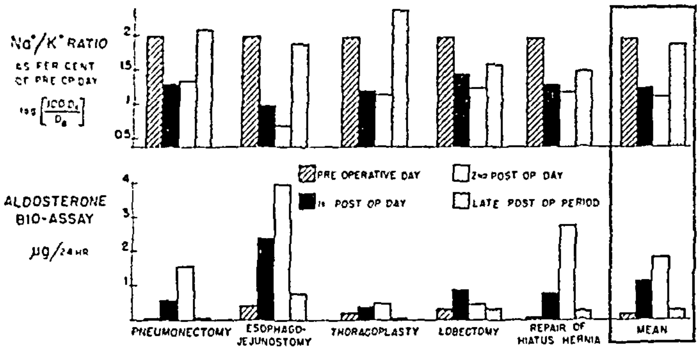

Fig. 1.—Comparison between diminished sodium/potassium ratio and increased aldosterone level in urine of patients before and after operation.

Changes in Aldosterone.—In the lower scale of the graph (fig. 1) the changes in the amounts of aldosterone excreted before and after operation are represented, with the same pictorial representation as above. In agreement with Thorn and co-workers,[6] not much weight is attached to the *absolute* values in micrograms of aldosterone, since the methods for estimating aldosterone can at present be regarded only as roughly quantitative—this being in *consequence of* the different methods used by different workers for extracting the urine and for the bioassay or physicochemical estimation. However, figures obtained from the same patient before and after a certain treatment, with use of the same method of extraction and the same method of determination, lend themselves to a fairly reliable comparison.

It may be seen (fig. 1) that there is a postoperative increase in the excretion of aldosterone concomitantly with the fall of sodium/potassium ratio. There is at present sufficient evidence to justify the belief that an increase in the excretion of aldosterone means an actual increase in production thereof by the adrenal cortex. Because of the complexity of the method of bioassay, it was not feasible to carry out serial determinations of aldosterone levels throughout the whole postoperative period. For this reason a single value in the late postoperative period chosen as indicated above is plotted. Although further work is necessary to determine the daily postoperative changes in aldosterone output, it can at least be *said that* by the time the sodium/potassium ratio in the patient's urine returns to normal, the aldosterone value has also returned to its preoperative level. It is of interest that, in the patients studied, increased postoperative aldosterone excretion does not appear to depend to any important extent on either the nature and magnitude of the operation or the amount and composition of fluid administered intravenously during the operation or the immediate postoperative period.[5]

To sum up it may be stated that, although the present findings do not indicate that aldosterone is the only factor responsible for the electrolyte changes present after operation, it seems reasonable to conclude that increased production of aldosterone is one of the principal factors responsible for such changes. It has been suggested[7] that this phenomenon be named postoperative transient aldosteronism. This terminology seems to be justified, since it denotes a temporary occurrence and keeps uniformity with the terms primary and secondary aldosteronism.[8] Some of these findings have been subsequently confirmed by American[9] and European[10] workers. Although the activity of the electrolyte-regulating corticoid extracted from urine postoperatively was indistinguishable from that of aldosterone in the bioassay, there was no absolute certainty that it was aldosterone until the latter was subsequently isolated and identified chemically in urine collected postoperatively.[11]

Effects of Postoperative Aldosteronism on Electrolyte Redistribution

For the *sake* of simplification, the large reservoirs in figure 2 are intended to represent the total sodium and potassium contents of the body; the elongated ones represent the plasma contents. The junctions represent the glomeruli, as indicated in the illustration, and the ascending tubes the renal tubules.

Behavior of the Kidney Toward Sodium.—Under the influence of increased circulating level of aldosterone, practically all sodium which forms part of the glomerular filtrate is returned to the plasma. There is an efficient renal sodium conservation after operation.

Behavior of the Kidney Toward Potassium.—Aldosterone has the effect of diminishing the tubular reabsorption—and of probably favoring the active secretion—of potassium. Hence, under these conditions very little of the potassium which reaches the tubules is returned to the plasma. Were it not for the fact that potassium is drawn out of the cells, a fall of potassium in the plasma would rapidly occur, which naturally would be of the same magnitude in the extracellular fluid. However, in the long run, this compensatory mechanism is detrimental to the cells, since potassium is an indispensable element for their normal functioning. As the cell becomes impoverished in potassium, the latter is replaced by sodium in order to maintain osmolarity within narrow limits. This phenomenon is known as intracellular "sodium-shift." The terminal stage occurs when the further loss of potassium from the cells becomes incompatible with their life. At this point, the potassium level in plasma falls alarmingly, and unless such hypokalemia with intracellular potassium deficit is promptly corrected, death usually ensues. Since the plasma potassium is only a very small fraction of the total body potassium, the values of the kalemia by themselves are not reliable indicators of the status of potassium metabolism in the patient.

Clinical Implications

It seems only reasonable to postulate that any scheme for treating the patient postoperatively must take into account the phenomenon of postoperative transient aldosteronism. This does not imply that the phenomenon be considered prima facie as beneficial to the patient. The question of its teleological significance necessitates further investigation. This section is only concerned with clinical or experimental aspects of surgical trauma so far known to bear, somehow, a connection with aldosterone.

First, from what has been said it follows that after surgical trauma the regulatory mechanisms of the body are readjusted so as to retain sodium and favor the excretion of potassium. Curiously enough, almost half a century ago Evans[12] drew attention, in the columns of The Journal, to the fact that excessive quantities of salt were administered to the patient postoperatively. However, this observation aroused little interest, and only 15 years ago it was almost customary to administer indiscriminately three or more liters of sodium solution daily to patients in the postoperative period. The disclosure of the state of aldosteronism after operation provides a rational basis for restraint in the practice of overloading the patient with so-called physiological saline solution. Such overloading only contributes to the following undesirable effects: accentuation of postoperative nausea and malaise; edema in the wound, lung bases, or intestinal suture line, depending on the state of the kidney, the previous state of nutrition, and the amount of potassium-free fluid; hypoproteinemia and resultant edema and also intracellular "sodium-shift." To avoid confusion, however, it must be added that judicious administration of sodium will be still indicated in those patients who have suffered selective losses of this cation, but this does not apply to routine postoperative management.

Second, it has recently been shown[13] in animals that aldosterone increases the propulsive motility of the small intestine and that this action is not shared by other adrenocortical hormones. Although this does not necessarily imply that aldosterone is a specific agent against intestinal paralytic ileus, it gives us a hint that perhaps the state of postoperative aldosteronism is, after all, not entirely harmful.

Third, in experiments in dogs it has been shown[14] that there is an increased excretion of aldosterone in response to chronic hemorrhage. Here again, the resulting conservation of fluids points toward a teleological significance of the phenomenon of postoperative transient aldosteronism.

Fourth, from time to time reference is made in the medical literature to a form of postoperative acute adrenocortical insufficiency which can occur even with minor operative procedures. The syndrome is characterized by the sudden appearance of marked hypotension, with tachycardia unresponsive to administration of blood, fluids, electrolytes, or vasoconstrictors. It is most likely that postoperative aldosteronism is absent in these cases. Postoperative acute adrenocortical insufficiency has responded promptly to intravenous administration of hydrocortisone (cortisol). It does not seem unreasonable to suggest that, when aldosterone is available for clinical purposes, it certainly deserves a trial in the treatment of this syndrome to see whether it is as effective as, if not more than, hydrocortisone.

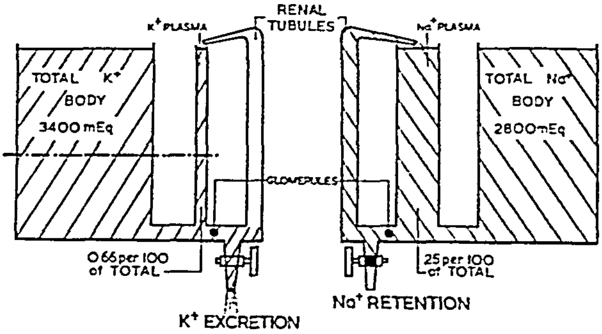

Fig. 2.—Schematic representation of kidney electrolyte function under state of aldosteronism.

Further research is still needed to elucidate the quasiphilosophical question of whether the state of postoperative transient aldosteronism has a definite teleological significance and, therefore, has to be respected in the postoperative period. Another question of interest may be formulated in the following terms: is postoperative transient aldosteronism an obligatory, inevitable response after surgical trauma, or may it be avoided, if indicated, by appropriate nutritional care of the patient, or by pharmacological means?

very little contrast density of the left kidney. The arrangement of the radiopaque material in the wall of the aorta was quite irregular, so that some areas appeared unusually dense and others much less so. The same applied to the common iliac arteries. Contrast medium was noted in the wall of the sigmoid colon, and the inferior mesenteric artery was markedly narrowed, with "hold-up" of dye in this vessel.

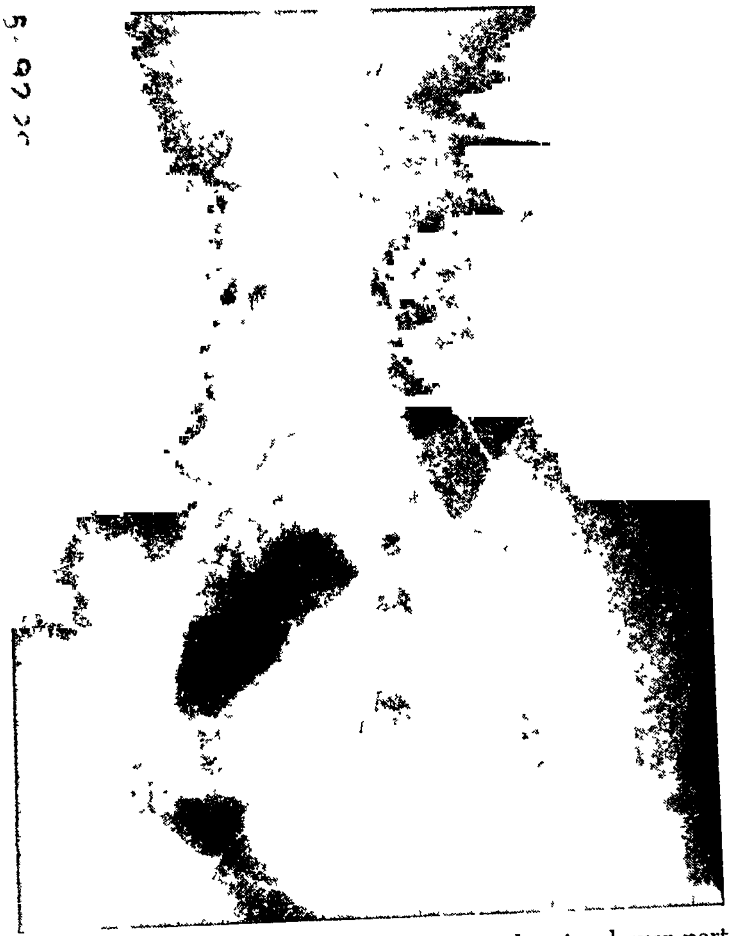

Fig. 1.—First roentgenogram in series, showing lower part of abdominal aorta and its major pelvic branches.

Within 24 hours after aortography, the patient developed severe left lower quadrant abdominal pain, melena, and abdominal distention. A roentgenogram of the abdomen now revealed a moderate amount of gas in the colon, with no abnormal distention but abrupt interruption of the column of gas. The walls of the lower descending colon and sigmoid were abnormally dense. These findings were interpreted as probably representing the earliest manifestations of infarction of the distal portion of the colon.

An emergency exploratory laparotomy was promptly performed. Examination of the peritoneal cavity disclosed the lower aorta to be thickened and severely arteriosclerotic, with no palpable pulsation. The superior left colic and mesenteric arteries were calcified, exceedingly sclerotic, and obviously thrombosed. There was gangrene of the entire distal large intestine extending from the distal transverse colon up to and including the rectum. The left ovary and the right ovary and fallopian tube were necrotic. Inasmuch as it seemed possible that the anal orifice could be saved, a classic abdominoperineal resection was not performed. Instead, resection of the involved intestine was carried out, as well as left oophorectomy and right salpingo-oophorectomy; a permanent transverse colostomy was established, and the peritoneal floor was closed. A roentgenogram of the resected intestine showed a large quantity of contrast medium present in the wall of the specimen.

The postoperative course was stormy, and the patient's convalescence was marred 17 days after laparotomy by wound dehiscence. She improved steadily thereafter, however, and was discharged in satisfactory condition 41 days after performance of the aortography.

Comment

A serious complication following a diagnostic procedure should logically be followed by critical analysis in an effort to determine any possible iatrogenic contributing factor. The first and foremost question is: "Was there a strictly valid indication for the procedure?" In a recent editorial, Schumacker[9] delved into the abuse of diagnostic aids. Many authors have admitted in retrospect that aortography is perhaps being employed in too many conditions where the conscientious application of physical diagnosis would as readily reveal the underlying pathology. Crawford and co-workers[6] have questioned the necessity for aortography in a majority of patients with aneurysms and occlusive disease of the abdominal aorta.

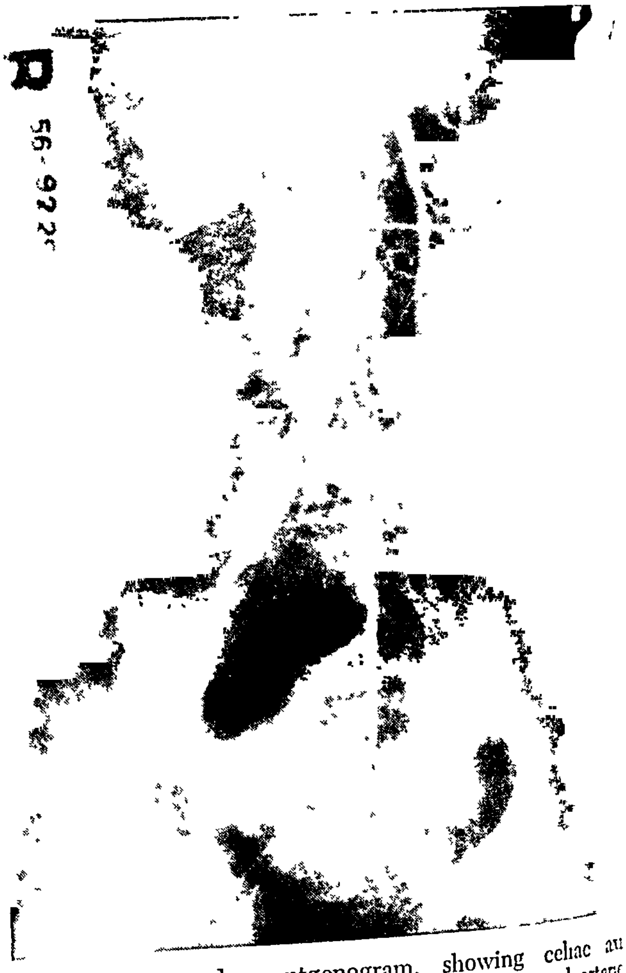

Fig. 2.—Second roentgenogram, showing celiac an superior and inferior mesenteric arteries, and renal arteri

Another question is whether flaws in techniqu were responsible for the ensuing accident. Smit and associates[10] reported that they inadvertentl injected only the superior mesenteric artery on se eral occasions without ill-effects. They mentione that mesenteric thrombosis eventuates if any one o a combination of the following factors exists: (

too great an injection pressure, (*b*) too large a volume of contrast material, and (*c*) the use of too toxic and irritating a contrast medium. To these items other authors have added the level of aorta which is penetrated. The choice of the latter is complicated and depends in part on the segment of aorta which one wishes to investigate. Dos Santos and co-workers[5] cautioned against inserting the needle in the area between T-12 and L-2. This route avoids the origin of the superior mesenteric artery but does not decrease the likelihood of perfusion in the inferior mesenteric artery, which usually arises at the level of the body of L-2 or L-3. Counter to this admonition is the recommendation of Reagen and Carroll[11] and of Smith and co-workers[10] that the injection be done above the celiac axis, that is, T-12. A lessened hazard of mesenteric thrombosis has not been substantiated by use of either of these approaches. In reviewing the films after aortography, it is our belief that the following sequence of events was responsible for the pathological findings:

On injection (fig. 1), the contrast material was divided into two portions. The major portion of the material was injected into a false channel outside the true lumen of the aorta. This was probably initiated when the tip of the needle entered the sclerotic aortic wall and lifted a sclerotic plaque. This created a new plane, and the contrast medium dissected along it. The left common iliac artery was filled by contrast medium flowing through the true lumen of the vessel. The inferior mesenteric vessel was simultaneously filled from the true lumen of the aorta. Immediately after the filling, the orifice of this vessel was occluded by the dissection occurring in the aortic wall.

One-half second later (fig. 2), the true lumen of the aorta above the point of dissection filled, and the renal arteries, superior mesenteric artery, and celiac axis became visible.

All of the contrast medium passed out of these vessels except for an undiluted dense collection in the area of dissection (fig. 3). There was also noted a persistence of filling of the right common iliac artery. This was presumably due to perilumenal dissection which occluded the lumen and prevented emptying of the vessel in the normal manner. This may well explain the resulting gangrene of the right fallopian tube as due to a compromised hypogastric circulation. At this time the wall of the descending colon became visible, indicating that the contrast medium had extravasated into the wall of the intestine. The inferior mesenteric artery remained filled, indicating infarction had already occurred and no blood was entering the vessel.

The degree of irritation produced by the radiopaque medium is of significance. Most of the fatalities accompanying translumbar aortography have occurred when inorganic iodides were used. An exception was the truly remarkable case, described by Joyeux and co-workers,[12] in which the patient suffered a colocolic intussusception following thrombosis of a tributary of the inferior mesenteric artery. Three weeks after aortography was done the patient spontaneously expelled three segments of colon. The eliminated fragments consisted of cylinders of large intestine complete with appendices epiploicae! Histological study revealed gangrene, but with all intestinal layers intact, from mucosa to serosa. Melick and others[13] investigated the effect of various organic and inorganic iodides injected directly into the superior mesenteric artery of dogs so that dispersion of the dye was almost completely into the intestines. They found that the injection of sodium iodide invariably produced hemorrhage, cyanosis, spasm, and gangrene of the intestines. The organic contrast mediums produced only mild spasm and slight cyanosis without any serious intestinal changes. Baccaglini and Ballarin[14] demonstrated rather marked microscopic inflammatory changes in the mesenteric vessels after the injection of sodium iodide in dogs. Sodium iodide has not been used in aortography for the past few years. While the organic compounds are admittedly less irritating, the occurrence of gangrene of the intestine in the case reported here attests to their not being altogether free from danger. Moreover,

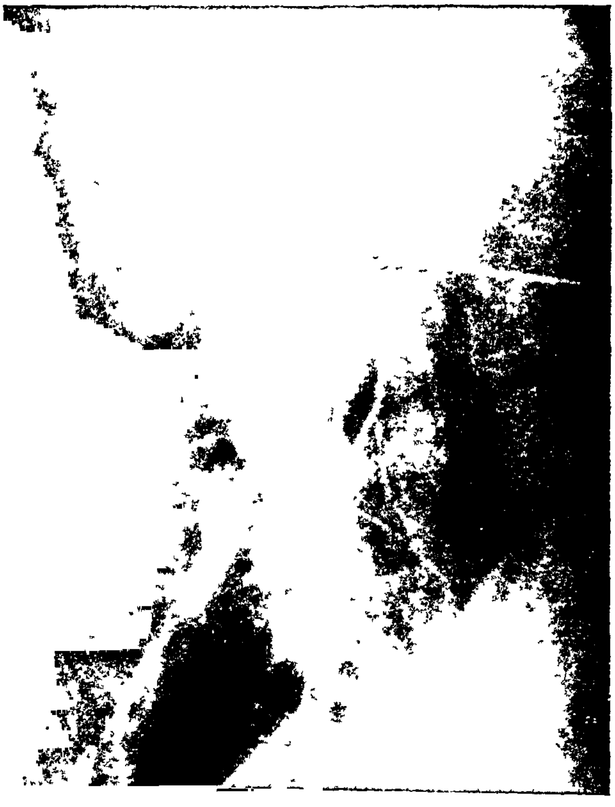

Fig. 3.—Last roentgenogram in series, showing density of right with little contrast density of left kidney.

renal and spinal cord damage have been reported irrespective of the type of contrast medium employed.

The prevalent consensus is that not more than 25 ml. of medium should be used per study and that repeated injections should be avoided. In the first account of a death from mesenteric artery thrombosis after aortography, Wagner and Price[15] advocated a test injection of a small diluted dose of medium just sufficient to enable adequate visualization, as determined by "wet plate" reading. If the roentgenogram of the preliminary injection reveals the needle to be in the desired location, a regular aortogram can then be taken. The same authors also pointed out that in some instances the "scout film" might enable sufficient visualization that one could forego a second injection with a more concentrated solution or larger dose. Walter and Goodwin,[16] McAfee and Willson,[17] and Osius[18] reported instances in which injection of a full dose of radiopaque material into the mesenteric vasculature was obviated when this technique was employed.

Summary

A case of gangrene of the lower half of the large intestine and of the ovaries occurred consequent to translumbar aortography. The patient survived after prompt resection of the necrotic viscera. This is the first report of concomitant thrombosis of mesenteric and ovarian vessels following aortography.

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NUTRITIVE VALUE OF FISH.—Market-fresh samples of various species of fish, including shellfish, which are commonly consumed in New England, were analyzed qualitatively for amino acids and quantitatively for nicotinic acid, riboflavin, vitamin B_{12}, total nitrogen, and total solids. A small number of canned samples was also analyzed. The edible portion of the fish muscle, blended in a Waring blender, was used for analysis. . . . The results indicate, in general, the high nutritive value of these marine species. Total protein is particularly high in halibut, mackerel, salmon, swordfish, lobsters, shrimp, canned salmon, and tuna. The lower total protein results exhibited by the other species are, for the most part, accounted for by higher moisture contents. As a source of nicotine acid, the following species can be considered as equal to or better than beef: halibut, mackerel, salmon, swordfish, and tuna. Haddock and shrimp are also good sources of this vitamin. Haddock roe, mackerel, smelts, clams, oysters, salmon, and tuna apparently are equal to beef as a source of riboflavin. The species showing the highest vitamin B_{12} contents include haddock roe, mackerel, salmon, smelts and, particularly, clams and oysters.—A. E. Teeri, M. E. Loughlin, and D. Josselyn, *Food Research*, March-April, 1957.

PENICILLINASE TREATMENT OF ACUTE RENAL INSUFFICIENCY DUE TO PENICILLIN HYPERSENSITIVITY

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The reported incidence of hypersensitivity reactions to penicillin is variable, but this reaction probably occurs in at least 2% of patients receiving this drug.[1] The reaction may assume many forms but usually includes urticaria or some other type of cutaneous eruption. In addition, about half of the patients develop a serum-sickness type of reaction, with fever and joint manifestations. Unusual reactions include purpura and vasculitis. Anaphylactic shock is not infrequently encountered, and many fatal cases are probably not reported.

Renal manifestations of hypersensitivity are rarely encountered.[2] Spring[3] reported a nephrotic syndrome accompanying a purpuric eruption, and one case of renal shut-down has been reported by Grassi and Catalano[4] in the Italian literature. Of a series of 84 patients with acute renal failure of diverse etiology, one case is attributed to a penicillin reaction, although no details are reported.[5] Our case of penicillin hypersensitivity is unusual because of the occurrence of acute renal failure and is of particular interest because of the response to a specific therapeutic agent, penicillinase. ACTH, prednisone (Meticorten), and antihistamines had been ineffective in controlling the manifestations of hypersensitivity in this patient.

Report of a Case

A 65-year-old male was admitted to the Richmond Memorial Hospital Jan. 19, 1958, because of thrombophlebitis, severe cellulitis, and erysipelas of the right leg. A superficial ulcer of the right heel had been present for three weeks prior to admission. The patient had received parenterally given penicillin for an infected finger two years previously without untoward incident.

On admission, temperature was 104 F (40 C), and pulse rate was 100. The sensorium was clear, and the patient was moderately dehydrated. The skin was rough and dry but of normal color. The right foot, ankle, and lower leg were swollen, red, hot, and tender to a level near the upper third of the calf, where a sharp line divided the inflamed area from normal-appearing skin. A draining ulcer, 3 cm. in diameter, was present on the right heel. Other pertinent findings included marked obesity, blood pressure 200/100 mm. Hg, and normal fundi. Many teeth were absent and the remainder were grossly carious and infected. The heart and lungs were normal. The abdomen was markedly obese, and no structures were palpable. The genitalia were normal. Rectal examination showed a smooth, moderately enlarged prostate gland. There was no significant lymphadenopathy.

Initial laboratory studies showed a white blood cell count of 16,000 per cubic millimeter, with 90% polymorphonuclear cells; the hemoglobin level was 13.7 Gm.%. Urinalysis was completely normal. The blood urea nitrogen (BUN) level was 25 mg.% and the fasting blood sugar level 95 mg.%. The Wintrobe sedimentation rate was 38 mm. in one hour. An electrocardiogram was interpreted as showing left ventricular strain, and chest x-ray was not remarkable except that the cardiac silhouette was at the upper limits of normal. X-ray of the right foot and ankle showed soft tissue swelling without bone involvement.

Therapy was started with 400,000 units of procaine penicillin G, 0.5 Gm. of dihydrostreptomycin-penicillin (Combiotic) twice a day, and 250 mg. per day of diphenhydramine (Benadryl) in divided doses. The right leg was elevated, and continuous hot boric acid dressings were applied. The leg began to improve almost at once, and the temperature fell to normal in 48 hours. However, on the third hospital day the patient became restless, confused, and uncooperative, and it was necessary to apply side rails to keep him in bed. On the sixth hospital day the patient's temperature rose to 101 F (38.3 C) rectally. Urinalysis at this time showed 75 mg.% of albumin and 45 red blood cells and occasional white blood cells per high-power field. Forty-eight hours later an urticarial reaction appeared on the thighs and rapidly spread over the entire body surface. The skin eruption became reddish purple and was studded with 0.5 to 1 mm. superficial pustules. The rash was accompanied by severe pruritis which was not controlled by symptomatic medication.

The urinary output was scant on the fifth and sixth hospital days, and no urine was passed on the seventh hospital day; 200 cc. was voided at one time late on the eighth hospital day. With the recurrence of fever on the sixth hospital day and the appearance of abnormal urine, dihydrostreptomycin-penicillin was withdrawn. The patient was then given tetracycline phosphate, 1 Gm. per day, and the dose of diphenhydramine was increased to 400 mg. per day.

At the height of the oliguria on the eighth hospital day, the patient had become stuporous and responded poorly to even vigorous stimuli, and occasional coarse tremors appeared. Respiration was shallow and stertorous. The pulse was rapid and of poor quality, although the blood pressure remained stable. BUN level had risen to 76 mg.%, and the urine contained 150 mg.% of albumin, with 30 red blood cells and 5 white blood cells per high-power field. The white blood cell count was now 28,000 per cubic millimeter, with 94% polymorphonuclear cells. The carbon dioxide level was 18, sodium 128, potassium 5.9, and chloride 105 mEq. per liter.

Prednisone and ACTH were administered but failed to affect the rapid deterioration of the patient's condition. At the height of oliguria he was, therefore, given a single intramuscular injection of 800,000 units of penicillinase (Neutrapen). ACTH was withdrawn but prednisone therapy was continued. In the 8 hours after the administration of pencillinase, the urine output was 50 cc., but in the next 24 hours the urine volume was 1,285 cc. Eight hours later an additional 1,500 cc. had been passed and thereafter the urine output averaged approximately 3,000 cc. per day. The BUN level reached a peak of 123 mg.% the day of the administration of penicillinase and within 36 hours it had fallen to 80 mg.%. The urine at this time was loaded with dark granular and cellular casts which were not present previously or subsequently on repeated urinalysis.

From the Medical Service, Richmond Memorial Hospital and the Medical College of Virginia Hospital.

Within 24 hours after the administration of penicillinase, the pulse and respiration improved markedly and the skin lesions began to fade. Desquamation of superficial layers of the epidermis appeared and continued as the skin returned rapidly to normal. As diuresis progressed, the BUN level fell steadily and serum electrolytes returned to normal. On Feb. 18, 1958, 30 days after admission, the BUN level was 18 mg.% and urine was normal. The improvement in the affected leg, after antibiotic treatment, continued without modification during the hospital course. At the time of discharge, the right leg was normal except for minimal erythema and slight edema. The ulcer of the heel had closed.

Comment

Severe acute renal insufficiency with oliguria from any cause is invariably associated with the rapid development of life-threatening uremia. In most instances, the etiological factors are known, and once damage has occurred little can be done except to attempt to maintain homeostasis until regeneration of tubular epithelium occurs. In cases where insults to the kidney continue for a protracted period (e.g., peritonitis) the outlook for return of renal function is not good. In the unusual case in which the patient reacts to penicillin with a severe renal lesion, it may be anticipated that the renal insult will continue as long as penicillin is present. Moreover, since urinary excretion is the chief method of penicillin elimination, high penicillin levels will be particularly prolonged when renal function is very poor. It is in such instances that an agent capable of neutralizing or destroying the offending substances is of untmost importance.

In 1940, the enzyme, penicillinase, prepared from various bacteria, was shown to be effective in destroying penicillin in vitro.[6] Recently, Becker[7] described the effect of penicillinase derived from Bacillus cereus upon penicillin circulating in humans. It was shown that penicillinase was well tolerated and that a single injection was capable of destroying all detectable circulating penicillin for several days, even though the patient continued to receive 800,000 units of penicillin twice daily. It appears, therefore, that penicillinase is a highly specific and effective agent for rapidly destroying penicillin in vivo and should be of value in alleviating penicillin reactions. In instances where difficulty in the elimination of penicillin is encountered or where long-acting penicillin has been administered, penicillinase should be particularly useful.

Our patient was admitted for treatment of a serious infection which could be anticipated to respond promptly to appropriate penicillin treatment. However, in spite of a gratifying response of the primary infectious lesion, the patient developed a nearly fatal penicillin reaction which included acute renal insufficiency as well as an exfoliative dermatitis. While acute renal failure may complicate many severe systemic illnesses, particularly when accompanied by shock, it is highly probable that the renal manifestations here reflect a penicillin reaction within the kidney, rather than a shock effect.

Significant hypotension did not occur in this patient, but profound urinary depression did occur concurrently with the skin eruption. Within a few hours of the administration of penicillinase, profuse diuresis supervened and the BUN level fell promptly. In contrast, during the course of usual oligurias, the tendency is for the urine volume to increase gradually over several days and the BUN level to continue to rise during the first few days of diuresis.

Thus, it appears here, from the circumstances surrounding the onset of oliguria, from the behavior of the urine volume, and from the trend of the BUN, that this case of renal insufficiency was a result of renal penicillin hypersensitivity, which was quickly alleviated by penicillinase. There was a dramatic change from practically no urine output to a state of adquate renal function, which would not be anticipated in the more common types of renal failure.

One can only speculate regarding the histopathology which was present in this case. Inasmuch as the return of function was very prompt, it would appear likely that there had been no extensive destruction of the tubular epithelium or vasculature at the time penicillinase was administered. The red blood cells and protein, found in the urine prior to treatment, are suggestive of a glomerulitis. The profusion of casts, found immediately after the administration of penicillinase, suggests that many nephrons were obstructed by protein precipitates and that this obstruction may have been relieved. Resolution of interstitial renal edema and subsidence of glomerulitis could have produced the results observed.

Summary and Conclusions

In clinical practice, a variety of penicillin sensitivity reactions are encountered frequently, but manifestations of renal hypersensitivity are rare. A case of acute renal failure resulting from penicillin hypersensitivity responded to penicillinase. The patient was given penicillin therapy for cellulitis and erysipelas. The infection improved but the patient developed a toxic reaction and exfoliative dermatitis and became uremic. Diphenhydramine (Benadryl), ACTH, and prednisone (Meticorten) were ineffective. The administration of 800,000 units of penicillinase (Neutrapen) was followed by profuse diuresis and rapid improvement.

Acute renal failure is a grave situation when the precipitating insult to the kidneys is continuous. This circumstance obtains when renal failure results from penicillin hypersensitivity, since the offending substance is very slowly eliminated and its harmful action persists. Employment of a specific and highly effective agent, penicillinase, for the destruction of penicillin, in our case, resulted in rapid improvement and gives promise of being of great value in similar situations. Since the renal response to penicillinase was so prompt, it is likely that no severe structural renal les

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A TESTICULAR SHIELD

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The amount of radiation delivered to the testes in x-ray examinations must be kept as small as possible, consistent with the clinical needs of the patient. Important means of accomplishing this are the elimination of unnecessary examinations and careful coning of the x-ray beam; but, even when coning is carefully done, the testes receive a relatively large dose during the making of such films

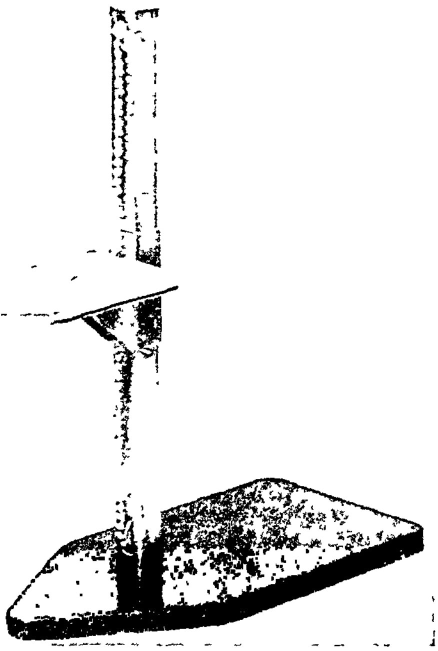

Fig. 1.—Testicular shield.

For several months we have been employing improvised shields, and recently our experimental shop has produced the instrument illustrated in figure 1. It consists of a ½-in.-thick Bakelite base with felt cemented to its undersurface. Rising from this base is a ¾ by ¾ by 15 in. hollow steel post on which rides a bracket that carries the shield. Within the post is a 1-lb. lead weight attached to the bracket by light cable chain passing over sheaves at the upper and lower ends of the post. The shield itself, illustrated in figure 2, is an assembly of 1 mm. of aluminum, 1½ mm. of lead, and 6½ mm. of Lucite (polymerized methyl methacrylate). This assembly is fastened to the bracket with oval-headed machine screws anchored by acorn brass nuts. The Lucite serves two purposes. It protects the printed instructions attached to the upper surface of the lead and projects 4.8 cm. beyond the

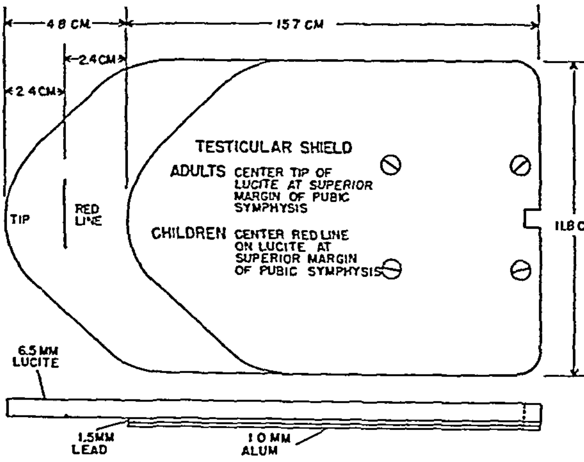
4.8 CM
15.7 CM
2.4 CM
2.4 CM
TESTICULAR SHIELD
ADULTS CENTER TIP OF LUCITE AT SUPERIOR MARGIN OF PUBIC SYMPHYSIS
CHILDREN CENTER RED LINE ON LUCITE AT SUPERIOR MARGIN OF PUBIC SYMPHYSIS
TIP
RED LINE
11.8 CM
6.5 MM LUCITE
1.5 MM LEAD
1.0 MM ALUM

Fig. 2.—Diagram of shield, top and side views.

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JAUNDICE ASSOCIATED WITH NORETHANDROLONE (NILEVAR) ADMINISTRATION

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A new anabolic steroid, norethandrolone (Nilevar), has recently been introduced for clinical use. This drug has been used successfully to reduce the hypercalcinuria associated with paralytic poliomyelitis.[1] Norethandrolone, 17α-ethyl-17-hydroxy-19-nor-4-androsten-3-one, is structurally intermediate between testosterone and estradiol. It has been shown to be a potent agent in reducing and reversing nitrogen catabolism.[2] However, at this service two of seven patients who received 1 mg. per kilogram of body weight per day of the drug over a period of several months developed jaundice.

Report of Cases

Case 1.—A 34-year-old engineer developed bulbospinal poliomyelitis in September, 1956. He required part-time respiratory aid. He was started on norethandrolone therapy, 20 mg. three times a day, on Dec. 20, 1956. He received this dosage intermittently over a period of 19 weeks, taking the drug for 14 weeks and being without it for one 3-week and two 1-week periods. On April 24, 1957, jaundice became apparent clinically, but norethandrolone therapy was continued until May 1, since no drug reaction was anticipated. By May 1, the serum bilirubin level had risen to 13.0 mg. per 100 cc. and the serum alkaline phosphatase level was 6 Shinowara units. Norethandrolone was withdrawn, but the serum bilirubin level continued to rise for four weeks until it reached 30 mg. per 100 cc. and the serum alkaline phosphatase level rose to 12 Shinowara units. The cephalin flocculation, thymol turbidity, and serum protein level remained normal. Bile and urobilinogen appeared in the urine. The urinary creatinine level increased from an average, before jaundice was evident, of 850 mg. per 24 hours to 1,450 mg. per 24 hours. Anorexia and intense itching were present at the height of the jaundice. Neither the liver nor the spleen was palpable at any time during the period of jaundice, so liver biopsy was not believed to be warranted. The serum bilirubin level declined during the six weeks after this episode to 0.9 mg. per 100 cc. The clinical course was otherwise benign during and after the jaundice, and the patient's muscle strength improved steadily as muscle function returned. As of mid-August, 1957, there were no apparent sequelae to the jaundice, and the urinary creatinine level had returned to an average of 800 mg. per 24 hours.

Case 2.—A 24-year-old man developed bulbospinal poliomyelitis on Aug. 29, 1956, and required a respirator for a short time. He was quadriparetic. He was started on norethandrolone therapy, 20 mg. three times daily, on Dec. 20, 1956. This was continued for 22 weeks, except for five weeks when the therapy was interrupted in order that we might observe the metabolic effects of withdrawal of the drug. On June 20, 1957, it was noted clinically that the patient was jaundiced, and the serum bilirubin level at that time was 3 mg. per 100 cc. This rose to 8.2 mg. per 100 cc. over the next week, even though the drug had been withdrawn promptly after the jaundice was noticed. The serum alkaline phosphatase level was 6 Shinowara units, and bile and urobilinogen appeared in the urine. The urinary creatinine level increased from a level before onset of jaundice of approximately 900 mg. per 24 hours to 1,200 mg. per 24 hours. The patient remained totally asymptomatic. Results of cephalin flocculation, thymol turbidity, and serum protein tests were normal. The liver, spleen, and lymph nodes were not palpable. There was a gradual subsidence of the bilirubinemia over the next four weeks. Urine bile, urobilinogen, and the increased creatinuria also subsided.

Comment

Jaundice similar to that observed in these two patients occurs with methyltestosterone[3] and chlorpromazine therapy.[4] With the latter drug, the jaundice and altered alkaline phosphatase level appear early and are considered to be hypersensitivity reactions. With methyltestosterone, on the other hand, jaundice appears late, after a prolonged course of the drug. Methyltestosterone therapy has also been reinstituted in the same patient without reappearance of the jaundice. Laboratory studies in patients suffering from reactions to methyltestosterone reveal an intense bilirubinemia with mild elevation of the serum alkaline phosphatase level. Bile and urobilinogen appear in the urine. Creatinuria and increased creatininuria have been described also.[5] No alteration is evident in other liver function studies. When liver biopsy has been done, the picture has been that of bile stasis with accumulation of pigment in the canaliculi and in the capillaries of the central portion of the lobule.[6] There has been no obstruction in the larger ducts. The production of jaundice with the methylation of C-17 by methyltestosterone (as distinct from the nonmethylated C-17 in testosterone, where jaundice has not been described) led to the speculation[3a] that metabolic degradation of methyltestosterone interfers with enzyme systems in the liver.

The incidence of jaundice during the administration of methyltestosterone is extremely low and apparently only associated with prolonged usage.[4b] Such jaundice is usually benign and asymptomatic. Koszalka reported the 19th case in the literature[3c] in which case death, probably attributable to methyltestosterone, occurred in an elderly man.

The clinical similarity in the development and course of jaundice between the two cases reported herein and those cases due to methyltestosterone is striking. Norethandrolone also has a substituted C-17 carbon, although the radical is an ethyl group. As of July, 1957, five cases of jaundice in subjects

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taking norethandrolone had been reported to the manufacturers,[7] indicating that bilirubinemia is a potentially frequent reaction to this drug.

Summary

Two cases of temporary jaundice occurred after the administration of norethandrolone (Nilevar), 1 mg. per kilogram of body weight, for periods of 14 and 17 weeks. In both patients there was a marked elevation of the serum bilirubin level and a moderate increase in the serum alkaline phosphatase level. Bile, urobilinogen, and increased creatinine appeared in the urine. Symptoms were mild, and no permanent sequelae occurred. The drug was not readministered to these patients. The pattern and clinical course of the jaundice was like that seen after methyltestosterone therapy.

This study was supported by grants from the National Foundation for Infantile Paralysis and the National Institute of Neurological Diseases and Blindness, U. S. Public Health Service.

The norethandrolone used in this study was supplied as Nilevar by Dr. Robert Craig of G. D. Searle & Co., Chicago.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. Kautz, M.D., *Secretary.*

CURRENT STATUS OF THERAPY IN INFANTILE DIARRHEA

Robert E. Cooke, M.D., Baltimore

This paper is a brief review of the therapeutic problems of diarrhea in infancy, especially acute diarrhea. Practical aspects of treatment are presented rather than theoretical principles. Other sources should be consulted for information on basic problems such as bacterial resistance, pharmacology of antibiotics, water and electrolyte physiology, and gastrointestinal allergy.

The incidence of diarrhea in infancy and childhood remains relatively high, although modern therapy has markedly lowered mortality. Each year several hundred cases of diarrhea are treated at the Harriet Lane Home in Baltimore. Even in areas of high socioeconomic status, severe epidemics of diarrhea continue to occur in nurseries for newborn infants. The epidemiology and prevention of such outbreaks will be discussed, since specific antibacterial therapy represents a significant part of recommended prophylactic measures.

Diagnosis

Diarrhea may be defined as an increase in the volume of stools. However, the diagnosis of diarrheal disease cannot be made precisely, particular-

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From the Department of Pediatrics, Johns Hopkins University School of Medicine, Johns Hopkins Hospital.

ly in young infants, since considerable variation in the number and size of stools normally exists. Clinical criteria of illness such as apathy, change in appetite, cessation of weight gain, and signs of water loss must be evaluated in addition to the observation of bowel movements. Optimum therapy of diarrhea requires an etiological diagnosis, and the following outline presents such a classification of etiological factors. The term "acute diarrhea" applies to a solitary, abrupt episode of only a few days' duration.

Etiological Classification of Diarrhea in Infants

Acute

- Improper Feeding
  - Overfeeding
- *Mechanical*
  - Shunt
  - Partial obstruction
- Chemical
  - Accidental ingestion of heavy metals, boric acid, exotoxin
- Biochemical
  - Hypoadrenalism
- Infectious, parenteral
  - Viral
  - Bacterial
  - Fungal
- Infectious, enteral
  - Viral
  - Bacterial
  - Fungal
  - Protozoan

Chronic or Recurrent Acute

- Improper Feeding
  - Overfeeding
- Mechanical
  - Shunt
  - Partial obstruction
- Chemical
  - Accidental ingestion of heavy metals, boric acid, exotoxin
- Biochemical
  - Gastrointestinal alkalosis
  - Celiac disease
  - Cystic fibrosis of the pancreas
- Neoplastic, parenteral
  - Ganglioneuroma
- Neoplastic, enteral
  - Lymphoma
  - Polyposis
- Allergic, enteral
  - Milk
- Allergic, parenteral
- Psychogenic
- *Infectious, enteral*
  - Viral
  - Bacterial
  - Fungal
  - Protozoan
  - Parasitic
- Idiopathic
  - Regional ileitis
  - Ulcerative colitis

Improper feeding is now less commonly considered as a cause of significant diarrhea than it was several years ago. Overfeeding, particularly, seems to have diminished in frequency, as a more reasonable and restricted demand-routine is followed. Mechanical factors, especially partial intestinal obstruction, may predispose the infant to severe acute diarrhea. Inflammatory changes in the intestinal wall proximal to the site of obstruction lead to extreme hyperperistalsis, particularly if a pathogenic micro-organism is present. Severe enteritis represents one of the major complications in the management of megacolon (Hirschsprung's disease), and this diagnosis must be considered in infants with persistent diarrhea, even in the absence of constipation. Acute diarrhea in infants may be caused by the accidental ingestion of preformed toxic substances such as boric acid, excessive iron, or staphylococcic exotoxin. The latter problems are discussed in connection with the treatment of *enteric infection.*

Increase in the volume of stools may be associated in infants with infection in organs other than those of the gastrointestinal tract. Control of pneumococcic and streptococcic pharyngitis, otitis media, and cervical adenitis by penicillin therapy has reduced the incidence of this type of diarrhea significantly. On the other hand, enteric infections continue to occur with relatively high frequency. Micro-organisms of many varieties have been reported to produce acute infectious diarrhea in infants. Several viruses have been isolated from outbreaks in hospital nurseries. Recently, enteric cytopathogenic human orphan (ECHO) viruses have been incriminated. The preventive and therapeutic approach to such infections is similar to that for enteric bacterial infection, except for antibiotic therapy.

The bacteria which are considered enteric pathogens in infants are listed in table 1. Salmonella organisms have been demonstrated to contaminate nurseries for prolonged periods of time. Shigellosis, on the other hand, is generally a problem of older infants and children in whom finger-to-mouth and fly-to-food transmission plays a more important epidemiologic role. Pseudomonas organisms may be found in the stools of asymptomatic infants; however, they are considered a possible cause of diarrhea by most workers. Acute staphylococcic enteritis, complicating broad-spectrum antibiotic therapy, is observed less frequently in infants and children than in adults. The sudden onset of extreme hyperpyrexia and hypotension, which is refractory to blood or plasma transfusions and only partly responsive to hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone), given intravenously, and to levarterenol (Levophed) bitartrate, is

Table 1.—*Bacteria Producing Acute Infantile Diarrhea*

Group	Organism
Salmonella	choleraesuis, oranienburg, typhimurium
Shigella	sonnei, flexneri
Escherichia coli	subtypes O 11 B 4, O 55 B 5
Pseudomonas aeruginosa (?)	...
Staphylococcus aureus	...
Hemolytic streptococci	group D(?)

characteristic. Hemolytic streptococci, group D, have been thought to produce diarrhea in infants through the conversion of tyrosine to tyramine. Neonates are allegedly susceptible because of a deficiency of tyramine oxides. However, this theory lacks solid substantiation.

At present, pathogenic strains of Escherichia coli constitute the major problem in infectious diarrhea in infants. At least 20 serologically distinct types have been demonstrated to be responsible for nursery epidemics throughout the world. Early and rapid identification of these organisms is essential, so that specific therapy and prophylaxis may be instituted and spread prevented. The stool rather than a swab of the rectum should be cultured, since these organisms undergo intraluminal rather than intramural multiplication. MacConkey's eosin-methylene blue and blood agar plates are used. Colonies are typed by slide or tube agglutination or precipitin techniques before and after heating. Rapid and accurate identification of pathogenic E. coli is now possible through the use of fluorescein-labeled rabbit antiserum applied directly to smears of feces. Comparison of this technique with accepted methods of culture indicates that smears so stained may demonstrate live organisms that do not grow on mediums because of inhibition by antibiotics.

Therapy

The treatment of acute infantile diarrhea may be considered from three standpoints, antimicrobial therapy, fluid therapy, and dietary therapy.

Antimicrobial Therapy.—Since antimicrobial therapy depends upon a specific etiological diagnosis, every effort should be made to isolate a pathogenic micro-organism.

Amebiasis has been reported in infants even in urban areas in the United States. Acute severe diarrhea, intermittent fever, or a chronic celiac-like syndrome may be the clinical manifestation of infection. Review of the literature, rather than personal experience, indicates that several agents are effective. Fumagillin (Fumidil), 1 mg. per kilogram of body weight per day for 10 days, or diiodohydroxyquin (Diodoquin, Yodoxin), 120 mg. per kilogram of body weight per day for 20 days, may be given by mouth. Bacitracin plus iodine 12.5% in the form of tablets has been recommended in a dosage of 10,000 units per day for 14 days for infants weighing less than 7 kg. and 20,000 units for infants weighing 7 to 12 kg.

Candida (Monilia) albicans likewise is an unusual cause of diarrhea in infants, except as a rare complication of antibiotic therapy. Nystatin (Mycostatin), 100,000 units four times a day for seven days, should be given in addition to stopping administration of other antibiotics. If broad-spectrum antibiotics must be continued for other disease, a combination of tetracycline plus nystatin (Mysteclin) may be used. Amphotericin B (Fungizone) may be even more effective against fungi than is nystatin.

The chemotherapeutic agents which are recommended for specific bacterial infections are listed in table 2. Test-tube tests or disk-sensitivity tests should be used whenever possible to permit optimal antibiotic therapy. The treatment of Salmonella infection is relatively unsatisfactory. Usually symptoms are controlled by chloramphenicol (Chloromycetin) alone or chloramphenicol plus tetracycline. The combination is probably preferable. Positive stool cultures and, occasionally, blood cultures may persist for weeks.

By contrast, Shigella infection responds to a number of drugs. Symptoms of diarrhea and fever usually last only a few days, even in untreated patients. The carrier state may persist longer, and spread of organisms may be greater if no chemotherapy is given. Although sulfonamides have been used extensively, bacterial resistance develops rapidly in epidemics. A similar phenomenon occurs when streptomycin, given orally, is used. Chloramphenicol or tetracycline (Achromycin, Panmycin, Polycycline, Tetracyn, Tetracyn V), whether given parenterally or orally, leads to rapid clinical improvement and negative stool cultures, at least temporarily. Polymyxin B (Aerosporin) sulfate given by mouth in a dose of 10 to 20 mg. per kilogram of body weight per day for 10 days would seem to be the most effective agent, as far as eradication of organisms from the stools is concerned.

TABLE 2.—*Antimicrobial Therapy of Diarrhea*

Organism	Drug	Oral Daily Dose, Mg./Kg. of Body Weight
Salmonella	Chloramphenicol	100
	plus	
	Tetracycline	40
Shigella	Polymyxin B sulfate	10-20
	or	
	Chloramphenicol	100
	or	
	Tetracycline	40
Pseudomonas	Neomycin sulfate	100
	plus	
	Polymyxin B sulfate	10-20
Escherichia coli, group B	Neomycin sulfate	100
	plus	
	Polymyxin B sulfate	10-20
Staphylococcus aureus	Erythromycin (Ilotycin)	40
	plus	
	Chloramphenicol	100
	plus	
	Neomycin sulfate	100
Hemolytic streptococci, group D	Neomycin sulfate	100
	or	
	Polymyxin B sulfate	10-20

Of particular interest from the standpoint of nursery epidemics is the antimicrobial therapy of diarrhea caused by pathogenic E. coli. Neomycin

(Mycifradin) sulfate given by mouth in a dose of 100 mg. per kilogram of body weight per day for 14 days produces rapid clinical improvement in the patient and prompt reduction, but *not eradication*, of the pathogenic organisms in the stools. Although not yet tested extensively in clinical trials, the combination of neomycin and polymyxin B sulfates in vitro is more effective than either alone and is recommended as the most effective therapy currently available.

Fluid Therapy.—Diarrhea, regardless of etiology, leads to losses of water, sodium, and potassium. The replacement of these deficits and the administration of water and electrolytes to meet continuing normal and abnormal losses must be guided by clinical means. Physical signs of dehydration are more helpful than laboratory procedures in assessing deficiencies in volume of body fluids (dehydration). Determination of the serum concentration, carbon dioxide content, and nonprotein nitrogen (or blood urea nitrogen) level is particularly helpful in individualizing certain phases of treatment. Table 3 shows the approximate deficits that may be expected in moderately severe dehydration due to diarrhea, although considerable variation exists from one patient to another.

Of particular interest and importance are the findings in hypertonic dehydration. This disturbance is now seen commonly because of the frequent use of improperly made electrolyte mixtures or of concentrated milk mixtures of high renal solute load even in hot weather. The deficits of sodium and potassium are small, and usually there is an excess (negative deficit) of chloride within the body. Suggested programs for replacement of deficits of water and electrolytes are given in table 4.

Initially, extracellular volume is expanded rapidly by a relatively small amount of slightly hypotonic fluid (lactated Ringer's injection) in order to improve circulation and renal function. Blood is used to correct shock and severe anemia. It should not be administered until some expansion of extracellular volume has been effected. Intracellular deficiencies of water and electrolytes and remaining deficiencies of the extracellular space are replaced more slowly. In hypertonic dehydration (sodium >160 mEq. per liter), therapy must be administered cautiously. Rapid reduction in sodium concentration with excess water probably leads to cerebral edema. Although deficits of potassium are relatively small, this cation should be given, since the development of hypocalcemic tetany can thereby be prevented. Severe seizures, which frequently occur 24 to 48 hours after beginning therapy, may respond to small amounts of hypertonic saline solution (3 cc. of a 3% saline solution per kilogram of body weight given in one to two hours) if the usual anticonvulsants such as phenobarbital are ineffective. Congestive heart failure occurs occasionally with hypernatremia and requires careful but rapid digitalization.

TABLE 3.—*Deficits of Water and Electrolytes in Infants with Moderately Severe Dehydration Due to Diarrhea**

Dehydration, Kind	Water, Ml.	Sodium, mEq.	Potassium, mEq.	Chloride, mEq.
Isotonic	100-120	8-10	8-10	8-10
Hypertonic	100-120	2-4	0-4	—2-—6
Hypotonic	100-120	10-12	8-10	10-12

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* Figures given per kilogram of body weight.

TABLE 4.—*Deficit Therdpy of Infants with Moderately Severe Dehydration and Electrolyte Disturbance**

Dehydration, Kind	Solution	Ml./Kg. of Body Weight	Time Schedule from Onset of Therapy, Hr.	Route
Isotonic	Lactated Ringer's injection	20	0-1	Intravenous
	Blood†	10	1-2	Intravenous
	5 or 10% invert sugar (dextrose and fructose) or dextrose in water	40	2-8	Intravenous
	Lactated potassic saline injection	60		
Hypotonic	Lactated Ringer's injection	20	0-1	Intravenous
	Blood	10	1-2	Intravenous
	5% invert sugar or dextrose in lactated Ringer's *injection*	40	2-8	Intravenous
	Lactated potassic saline injection	60		
Hypertonic	Lactated Ringer's injection	20	0-1	Intravenous
	Blood	10	1-2	Intravenous
	5 or 10% invert sugar or dextrose in water	60		
	6th molar sodium lactate injection	20	2-8	Intravenous
	Potassium acetate	0.5		
	Calcium gluconate injection‡			

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* To be followed by usual maintenance fluid therapy plus replacement of abnormal losses.

† Not considered part of deficit therapy; for shock or anemia.

‡ To be used for signs of tetany.

Deficit therapy is followed by the administration of adequate fluid to meet the usual losses of water and electrolytes from the body as well as abnormal fecal losses. Stool losses range from 50 to 300 cc. per day in young infants, depending upon the severity of the diarrhea. Stool losses are best replaced by lactated potassic saline injection (Darrow's solution) diluted with an equal part of 5% dextrose in water. Menadione, 1 mg. per day, or other vitamin K derivative should be administered parenterally to combat hyperprothrombinemia, which is observed occasionally in severe diarrhea.

Dietary Therapy.—Oral feedings may be administered after cessation of profuse diarrhea, vomiting, and abdominal distention. A dilute water and electrolyte mixture (Harriet Lane Home mixture) should be given initially in amounts varying from 100 to 150 cc. per kilogram of body weight per day. This mixture contains the following ingredients: sodium chloride, 1.7 Gm.; potassium bicarbonate, 2.0 Gm.; and sucrose, 50 Gm. This mixture (1 unit) is added to one quart of water, or one quart of water is used, to which is added a powdered preparation of electrolytes (Lytren), given orally, so as to provide the following per liter of solution: sodium, 50 mEq.; potassium, 20 mEq.; calcium, 4 mEq.; magnesium, 4 mEq.; citrate, 35 mEq.; sulfate, 4 mEq.; chloride, 30 mEq.; phosphate, 10 mEq.; and lactate, 4 mEq. In mild cases not requiring hospitalization, such mixtures may be used for replacement of small deficiences of body fluids. Such therapy is more rational than the time-honored regimen of boiled skimmed milk. The latter fluid presents a high renal solute load at a time when extrarenal losses of water are high. Two dangers in the use of electrolyte mixtures are encountered. First, parents may use more than the recommended amounts of powder in home preparation, and hyperosmolarity (hypernatremia) may result. This difficulty may be obviated by using unit packaging such as the Harriet Lane Home unit. Second, more than 150 to 200 cc. per kilogram per day may be ingested, resulting in continuing diarrhea. Substitution of parenterally administered fluids for oral intake leads to prompt cessation of diarrhea in such patients.

Milk mixtures or milk substitutes are given in gradual increments in place of orally administered water and electrolyte mixtures as the volume of stools decreases. Since there is evidence that gastrointestinal permeability to whole protein is increased in the recovery phase of diarrhea, hypoallergenic mixtures such as hydrolyzed casein or soybean formulas are recommended. Although full caloric intake throughout the diarrheal disorder has been recommended by some authors, such a practice leads to increased stool losses of water and electrolytes and thereby prolongs and complicates parenteral fluid therapy. The use of nonspecific measures such as absorbing agents or demulcents is not indicated in diarrhea in infants. Diiodohydroxyquin, which has been shown to be effective in mild chronic or relapsing diarrhea of unknown etiology, cannot yet be considered suitable for use in acute infantile diarrhea.

Preventive Measures

The physician is responsible not only for the care of the infant with diarrhea but also for the prevention of spread of the disease. Complete eradication of pathogenic organisms is not yet possible, but the chances for spread of infection are minimized by quantitative reduction in the number of pathogens in the environment. Careful handwashing technique and terminal sterilization have significantly reduced milk-borne infection. By contrast, air-borne infection is difficult to eradicate, particularly in the case of pathogenic E. coli, since prodigious numbers of these organisms may be excreted. Bacteriological study of air samples indicates that procedures such as changing diapers, making up bassinets, and weighing the infant lead to gross contamination of the environment if an infant is infected. In the presence of crowding, inadequate turnover of nursery air, and inexperienced personnel, spread of infection is inevitable.

Control of the number of pathogenic bacteria in the environment may be effected by administration of proper antibiotics. Neomycin and polymyxin B sulfates in the dosage recommended for therapy should be given to all infants in the nursery when pathogenic E. coli are recovered from patients with diarrhea. Such therapy not only protects the other infants but also prevents gross contamination of the physical facilities.

Chemotherapy cannot be used as a substitute for all other control measures, and nurseries must be closed when two or more cases of diarrhea are detected. All personnel should be tested and relieved from duty if they are carriers. Isolation techniques must be made more stringent and cross contamination reduced by minimizing movements of contaminated articles.

ESCHERICHIA COLI DIARRHEAS.—It is now widely recognized that certain specific strains of E. coli may cause infantile diarrhea (0127:B8, 0111:B4). The subject has been reviewed recently by Cooper, Walters and Keller, Stulberg and Zuelzer and others. It is perhaps significant that as early as 1927, Adam in Germany called attention to the role of E. coli in so-called alimentary intoxication in infants and children and much later the British and American clinicians and bacteriologists began to study the problem and recognize the significance of certain strains of E. coli as a cause of diarrhea. Outbreaks of diarrhea associated with the presence of E. coli are characterized by the sudden development of extreme abdominal distention, explosive onset of diarrhea and the presence of copious stools. Not all outbreaks of diarrhea in nurseries are due to pathogenic strains of E. coli. When, however, these cases occur it is important to recognize them because the strains are highly sensitive to neomycin.—C. S. Keefer, M.D., Food Poisoning, *The American Journal of Gastroenterology*, April, 1958.

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THE SURFACE AREA OF THE BODY

NOT MANY years ago a book on medical emergencies suggested for the treatment of diabetic coma the reestablishment of normal circulation by the intravenous administration of a saline-lactate solution. This solution was described in a footnote as being made from 400 cc. of "isotonic saline," 40 cc. of "molar Na lactate," and 560 cc. of distilled water. This mixture was to be administered at the rate of 800 ml. *per minute per square meter* of body surface. Unfortunately this suggestion assumed that, under emergency conditions, the physician would know exactly what was meant by "isotonic saline," that he would have no trouble in preparing a molar solution of sodium lactate, and that he would be able to calculate the rate at which the injection was to be made. Since the actual area of the body surface is difficult to measure even in the laboratory, a footnote referred the physician to an appendix, where he was informed that one square meter of human body surface is equal to 28 kg. of body weight. Thus, having ascertained the patient's weight in pounds, the physician was to convert it into kilograms, work the appendix backwards to obtain the patient's area in square meters, and ultimately arrive at the number of millimeters of solution to be injected into the patient per minute. To the average reader it seemed evident that the entire calculation might as well have been based on body weight in the first place and that the mention of body surface might only add confusion to the procedure.

The above is but one instance of the confusion concerning the concept of body surface area. The introduction of this concept by Rubner was a stimulating contribution to general physiology. Its subsequent development in the hands of others has been traced by Oliver, Graham, and Wilson elsewhere in this issue of THE JOURNAL (page 1211). Unfortunately, there has been a tendency to accept as an axiom what is proposed as a hypothesis. To describe the resulting fallacies in detail is out of the question here, but some of them have been analyzed in a paper by Tanner.[1] Taking cardiac output, oxygen consumption, plasma volume, glomerular filtration rate, and renal plasma flow as examples, Tanner has explained the fallacies which must result from an uncritical assumption that any of these quantities can be represented accurately on either a per-weight or a per-surface area basis.

The difference between the per-weight and the per-surface area bases is that the former is simple enough to permit incongruities to come to light promptly, while the surface area concept conceals them. Both bases start out with an assumption of direct proportionality that is contrary to fact, but when the resultant difficulty is recognized it can be corrected for. Oliver and his associates correct for it by admitting discontinuities in the relation of water requirement to body weight. The resulting discrepancies in children aged 1 and 5 are easily recognized and easily disposed of. But to use body surface area is quite a different matter; it is not measured but calculated. There is a danger in repeated allusions to something that is never seen, handled, or measured; one may come to believe it important when it does not even exist. There is also a danger in using mathematics and statistics to embroider a medical contribution; such embellishment does not make a paper scientific, and it may do the reverse; it may take a sharp-eyed scholar indeed to see through the camouflage of cosines and logarithms behind which some fallacies are entrenched. This concept of body surface area has an important place in the fundamental research, but it is not suited to use in most emergencies. It can best be introduced in situations where critical thinking and ample data specifically justify its use. At present, comparatively few situations of this sort appear to exist in the field of clinical medicine, and the physician as a practical measure must base his calculations as directly as possible on directly ascertainable data.

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[1] Tanner, J. M.: Fallacy of Per-Weight and Per-Surface Area Standards, and Their Relation to Spurious Correlation, J. Appl. Physiol. 2:1-15 (July) 1949.

DR. LOUIS M. ORR–PRESIDENT-ELECT

At the 107th Annual Meeting of the American Medical Association in San Francisco the House of Delegates elected Dr. Louis McDonald Orr of Orlando, Fla., President-Elect to take office as President in June, 1959, at the Atlantic City meeting. Dr. Orr was born Sept. 27, 1899, in Cumming, Ga. He received a bachelor of science degree in 1922 and his medical degree in 1924 from Emory University Medical School, from which he graduated near the top of his class and where he was a member of Caduceus and Asklepios honor societies and Phi Rho Sigma and Phi Delta Theta fraternities. While in medical school he was encouraged by Dr. Dan C. Elkin to seek a surgical house officership at Peter Bent Brigham Hospital, Boston, where Dr. Elkin had been a surgical resident.

Louis M. Orr, M.D.
President-Elect of the American Medical Association

In 1926, with a group from Peter Bent Brigham Hospital led by Dr. Elliott Cutler, Dr. Orr went to Cleveland to take over the old Lakeside Hospital, when Dr. George Crile moved to the present Cleveland Clinic buildings. He returned to Boston later and became a preceptee of Dr. Arthur L. Chute. In February, 1927, he opened an office in Orlando, Fla., where his brother was in business, and in December he married Miss Dorothy Brown, whom he had met while interning at Peter Bent Brigham Hospital. His son, Louis McDonald Orr Jr., is completing his second year in medicine at Emory University. His daughter, Doris, graduated from Mount Vernon Seminary in Washington, D. C., and will enter college in September.

When Dr. Orr was made a fellow of the American College of Surgeons in 1933, it was said: ". . . his recognition by the American College of Surgeons while yet so young in his profession is considered a tribute to his exceptional ability." Now he is a consultant in urology and director of postgraduate education at Orange Memorial Hospital in Orlando, a member of the American Association of Genito-Urinary Surgeons, American Urological Association, Southern Medical Association, Southeastern Surgical Congress, American College of Surgeons, International Society of Urology, Society of Nuclear Medicine, a founding member of the American Board of Urology, a past-president of the southeastern section of the American Urological Association, and an honorary member of Alpha Omega Alpha. He is on the consulting staff of the Institute of Nuclear Studies at Oak Ridge, Tenn. The Louis M. Orr Foundation for Cancer Research has an executive board composed of prominent Florida citizens.

Dr. Orr has been Vice-Speaker of the House of Delegates of the American Medical Association; Chairman of the Committee on Federal Medical Services, ex officio Member of the Council on Constitution and By-Laws, and a member of the Council on Medical Service. In addition to contributing much to medical literature, he has been active in the Florida Medical Committee for Better Government.

Through their gifts, Dr. and Mrs. Orr made possible the fourth blood bank in America, which was operated at the Orange Memorial Hospital until 1943, when all of the equipment was turned over to the central Florida Blood Bank. As a member of the board of directors of the U. S. Committee of the World Medical Association, Dr. Orr attended the 11th General Assembly in Istanbul, Turkey, in 1957.

Having entered the Army in 1942, later Colonel Orr became commanding officer of the 15th Hospital Center, with headquarters in Cirencester, England. He was awarded the Bronze Star medal and the British-American Liaison Board inscribed a formal expression of their indebtedness to him. A letter signed by the enlisted men under his command ends with these words: "Colonel Orr's genuine interest in the welfare and morale of the enlisted men is one of the finer memories that will live long after less pleasant remembrances of war and Army life sink into oblivion."

Dr. Orr was president of the Central Florida Civic Music Association for seventeen years. He is chairman of the Municipal Auditorium Committee, and formerly was chairman of the Loch Haven Park Board which has charge of a tract of land set aside by legislative act for cultural purposes. He was a trustee of Rollins College in Winter Park, Fla., from 1937 to 1951, and received its highest honor, the Algernon Sydney Sullivan award, in 1946. He is a member of the Country Club of Orlando, and the Colony Club of Mountain Lake.

Dr. Orr was one of the few medical officers who qualified as an expert rifleman in World War II. Hunting and fishing are his long-time enthusiasms. In his garden in Orlando are rare camellias which have won blue ribbons at many flower shows.

A vigorous fighter for the rights of the individual, Dr. Orr believes that the medical profession's greatest concern is to provide the best medical care possible to all patients. He believes this can never be done under a bureaucratic system.

DR. KRUSEN GIVEN DISTINGUISHED SERVICE AWARD

Dr. Frank Hammond Krusen, professor of physical medicine and rehabilitation, Mayo Foundation, University of Minnesota, Minneapolis, was given the American Medical Association's Distinguished Service award on June 23rd, during the annual meeting in San Francisco. His name was selected by the House of Delegates from three names submitted by the Board of Trustees, which had been screened from names proposed by the general membership of the Association. Dr. Krusen's award was given in recognition of his achievements in the field of physical medicine and rehabilitation.

Frank Hammond Krusen
Awarded Distinguished Service Medal

Dr. Krusen is Chairman of the A. M. A. Council on Physical Medicine and a member of the special committee of the Board of Trustees on rehabilitation. He is a graduate of the William Penn Charter Prep School and the Jefferson Medical College, Philadelphia. In 1931 he opened the new department of physical medicine at Temple University, a post he resigned in 1935 to take charge of a similar department at the Mayo Clinic, where he has remained. In 1938 he was installed as president of the American Congress of Physical Therapy. He is a Fellow of the American College of Physicians, past-president of the American Academy of physical Medicine, member of the Subcommittee on Physical Therapy of the National Research Council, and chief consultant on physical medicine to the Army surgeon general. He received the Annual Gold Key award of the American Congress of Physical Medicine and Rehabilitation in 1944, in 1953 the President's Physicians award for services to the handicapped, and in 1954 the Award of Merit from his native state of Pennsylvania. In 1955 he was appointed to the Minnesota State Board of Health, and in 1956 he was elected president of the International Federation of Physical Medicine to succeed the late Lord Horder of England. From 1949-1951 he was editor of the "Yearbook of Physical Medicine and Rehabilitation." Dr. Krusen was 60 years of age on June 26. He is married and the father of two children.

IS THE BABY BOOM ENDING?

Although the number of births in the United States still exceeds 300,000 a month, the total for the first quarter of this year was some 7,000 below last year. This small decline in the number of births has occurred less than nine months after the decline in the number of marriages. These two declines suggest but do not prove that the end of the baby boom is in sight. Because of the comparatively small number of births during the 1930's, the number of youths attaining marriageable age continues to be fewer than can be expected during the 1960's.

Doubtless the small decline in the number of births during the first quarter of 1958 and the earlier decline in the marriages is due in some measure to the business recession. To that extent, an increase in the number of both the births and marriages will depend upon improvement in business conditions. Forecasting business developments is somewhat beyond the scope of The Journal. We submit, however, that these recent declines in births and marriages should make one hesitate about predicting a population explosion in the United States as has been frequently predicted in recent years for the world as a whole. Much will depend on the number of second, third, and fourth order births; the publication of birth-order data lags two or more years. At the very least, until the trends of births and marriages become a little clearer we cannot conclude with any degree of firmness whether the present plateau is a prelude to a considerable decline or a mere interval in an irregular rise in births and marriages.

ORGANIZATION SECTION

CONFERENCES ON LABELING HAZARDOUS SUBSTANCES IN PACKAGED CHEMICALS

The growing demand for uniform legislation to require precautionary labeling of all chemical products which are not now so regulated was discussed at a legislative conference held on May 9, 1958, at the A. M. A. headquarters. Speaking to government, industry and medical representatives from approximately 40 national organizations, members of the A. M. A. Committee on Toxicology discussed the "Uniform Hazardous Substances Act" and compared it with other tentative legislation which has been proposed.

Attention was first focused on the general nature of the problem, as seen by the medical profession, public health officials, and the public, by remarks from a pediatrics representative and officials of the American Public Health Association and the National Safety Council. The principles, which the Committee employed in formulating the provisions of a model law for labeling all types of hazardous substances, were reviewed. A comparison of the model bill with other tentative legislative proposals followed.

An industry-wide label law conference, scheduled for July 25, 1958, under the sponsorship of the Committee on Toxicology was announced. The conference will discuss proposed legislation requiring the declaration of hazardous ingredients and warning statements on the label and in the accompanying literature of household, commercial, and industrial packaged chemicals. Over 100 organizations including representatives of trade associations, toxicity testing laboratories, chemical trade unions, and similarly interested groups are being invited to participate.

This is the second of several meetings which are to be held to discuss proposals for local and federal label laws. Attention will be focused on the "Uniform Hazardous Substances Act" which was recently drafted by the Committee on Toxicology to close the gap in label legislation. These meetings are being held in order to bring about a clearer understanding of what the model bill is intended to cover and the benefits to be derived from such legislation. Interested parties may obtain further information by contacting the Secretary, Committee on Toxicology, 535 N. Dearborn St., Chicago 10.

DR. SPRINGALL RESIGNS

Dr. Arthur N. Springall, Assistant Secretary of the Council on Medical Education and Hospitals, has resigned in order to become Director of Professional Services of the Veterans Administration Hospital in Oklahoma City on Aug. 1. During his five years with the Council, Dr. Springall has played an important role in its graduate medical education activities. During the past two years, he has coordinated the work of the field staff and the preparation of the Annual Directory of Internships and Residencies. He has served as Secretary and Administrative Officer of the Internship Review Committee and of the Residency Review Committees in Dermatology, Radiology, Preventive Medicine, and General Practice. The American Medical Association is deeply appreciative of his fine work and cooperation.

MINNEAPOLIS CLINICAL MEETING, DEC. 2-5, 1958

The program for the Clinical Meeting in Minneapolis, Dec. 2-5, 1958, is nearly complete. Applications for space in the Scientific Exhibit, however, will be accepted until Aug. 1. All applications should be sent to the Secretary, Council on Scientific Assembly, American Medical Association, 535 N. Dearborn St., Chicago 10.

CHANGE OF ADDRESS

If you change your address please notify The Journal at least six weeks before the change is made. Include the address label clipped from your latest copy of The Journal, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

COUNCIL ON MEDICAL SERVICE

STUDY OF PERINATAL MORTALITY AND MORBIDITY PROGRAMS IN THE UNITED STATES

PART 2

PHILADELPHIA STUDY OF FETAL DEATHS

The study of fetal deaths is an integral part of the total perinatal study in Philadelphia, and the Fetal Death Committee is one of three sponsored by the Philadelphia County Medical Society which are specifically devoted to the education of physicians and the reduction of maternal, neonatal, and fetal deaths through mortality studies. The Maternal Welfare Committee study was reported May 26, 1956, in The Journal as part of the series on maternal mortality studies. The experience of the Neonatal Study Committee is described in part 1 of this series in The Journal, June 28, 1958, page 1124.

History

Fetal death studies were begun in 1937 under the sponsorship of the Obstetrical Society of Philadelphia but were discontinued in 1941. The study was reactivated in 1951. Membership in the study committee included a chairman and three other obstetricians. The obstetrical society provided a small operating budget, and the Philadelphia County Medical Society and the Philadelphia Department of Public Health participated jointly in the project, furnishing various supplies and services. In 1954 this committee was expanded to include 12 obstetricians, and at that time it became an official committee of the Philadephia County Medical Society. These additional members were appointed by the president of the medical society upon the recommendation of the chairman of the committee.

Scope of Study

Fetal deaths occurring after 16 or more weeks' gestation (prior to 1954, 20 weeks) are included in the committee's study. A fetal death is defined as one in which there is no evidence of life after complete birth (no breathing, no action of heart, no movement of voluntary muscle). Birth is considered complete when the baby is completely delivered (head, trunk, and limbs), even if the cord is uncut and the placenta still attached.

Method of Operation

Case-finding and Collection of Data.—The hospital representative, a physician serving both the Maternal Welfare Committee and the Fetal Death Committee, is supplied with questionnaire study forms similar to those for the neonatal study and with instructions for preparing and submitting data on each fetal death that occurs in his institution. In addition, through cooperation of both state and local offices of vital statistics, fetal death listings are sent to the secretary in the Philadelphia Department of Public Health who also handles the maternal and neonatal mortality study forms. She notifies the hospital representative monthly of the fetal deaths for which no completed study forms have been received. This physician thus has knowledge of every fetal death occurring in his hospital, and, if the attending physician has not already filled in the information requested, the representative obtains it from the hospital records, the attending physician, and the resident or intern assigned to the case. This is done as quickly as possible, so that the fact will be fresh in the minds of those who attended the patient.

Processing of Data.—The completed questionnaires are reviewed by a physician, at the present time a member of the department of health, who screens the cases. Interesting and controversial reports are further screened by a four-member steering committee of the Fetal Death Committee. Selected cases are reviewed by all 12 members of the committee, and one or two cases may be chosen for presentation at the bimonthly combined meeting. Until 1955, monthly meetings were held jointly with the Maternal Welfare Committee. Currently, bimonthly meetings are conducted with the Neonatal Study Committee as well. These are open meetings attended by interested physicians, nurses, medical students, and members of the three committees. One or more selected cases of educational value are (with anonymity maintained) presented by a member of the committee or by the physician involved.

This is the second of a series of articles prepared by the Committee on Maternal and Child Care of the Council on Medical Service on perinatal mortality and morbidity study programs that are being conducted in various parts of the United States. Subsequent articles will appear in The Journal from time to time.

Committee members are W. L. Crawford, M.D., Chairman, Rockford, Ill.; R. B. Chrisman Jr., M.D., Coral Gables, Fla.; Philip S. Barba, M.D., Philadelphia; Harold S. Morgan, M.D., Lincoln, Neb.; Garland D. Murphy, M.D., El Dorado, Ark.; Howard A. Nelson, M.D., Greenwood, Miss.; J. L. Reichert, M.D., Chicago; Donald A. Dukelow, M.D., Consultant, Chicago; and Mr. George W. Cooley, Secretary, and Mr. Donald B. Berg, Research Assistant, Chicago.

Classification of fetal deaths is similar in method to that used by the Maternal Welfare Committee. It is recommended that this be done at individual hospital staff meetings before the questionnaire is submitted to the committee; space on the form is provided for this purpose. However, after reviewing the case, the committee may change the classification given by the informant. The deaths are classified as obstetric or nonobstetric and as preventable or nonpreventable. Responsibility for deaths considered preventable is charged to the physician or to the patient, and the preventable factors are listed. Some cases are classified as nonpreventable but with suspected preventable factors. These decisions are based almost wholly on clinical judgment, since thus far only 21% of the autopsies have demonstrated a specific pathological condition. It is the committee's opinion, however, that more autopsies should be sought and that pathologists should become more adept at recognizing fetal pathological conditions.

Follow-up and Use of Findings.—Findings from 1,000 sequential fetal death study cards were reported in *Surgical Clinics of North America* for December, 1954.[1] Other materials and reports have appeared from time to time in *Philadelphia Medicine,* the official bulletin of the Philadelphia County Medical Society. In 1955 a regular feature of this bulletin was a complete report of the bimonthly three-committee joint meeting, including presentation of at least one maternal, one neonatal, one fetal death, discussion of these cases, and analyses and final classifications. No attempt has been made, as yet, to notify attending physicians of the committee's decisions regarding their cases, but plans are being made for such a procedure. In the meantime, hospital staffs are encouraged to review the fetal deaths occuring in their institutions, and all interested persons are encouraged to attend committee meetings.

Results

One thousand reported cases (from May 1, 1951, to Aug. 31, 1952) have been tabulated. This represents a 76.4% return of completed study cards. Of the 1,000 cases, 302 were classified as preventable (101 by physician, 201 by patient), 688 as nonpreventable (including 85 with suspected preventable factors), and 10 as nonobstetric and nonpreventable maternal illnesses. Of the preventable fetal deaths, 31.7% were associated with prolonged labor and 19.8% with acute toxemia. Other causes included breech and transverse presentations, errors in technique, prolapsed cord, and diabetes. The 201 cases considered to have been preventable by the patient were so classified because the patients received little or no prenatal care. In more than 50% of these cases the cause or contributing causes of fetal death could not be determined. Among the other 50%, acute toxemia was the prime factor. Of the 85 nonpreventable cases with suspected preventable factors, 52 were associated with acute toxemia. Of the 603 other nonpreventable cases, 35% were nonviable late abortions in mothers who had had adequate prenatal care.

The reduction in the fetal death rate since 1937, as shown in the table, is in reality much greater than the reported figures because reporting of fetal deaths has become much more complete in recent years. The apparent increase in 1954 reflects a change in Pennsylvania law from 20 to 16 weeks as the maximum length of gestation for which no fetal death certificate is required.

Comments and Conclusions

The Fetal Death Committee believes that study committees such as this dramatize the need for action by individual physicians. Even the data required for the questionnaire help to emphasize possible errors to the attendant and the discussion of such cases is a helpful educational device. However, the members of the committee feel that employment of a professional investigator (preferably an obstetrician) would make its efforts more effective and would lead to greater accuracy in the study. Greater coordination of this committee's work with that of the other two study committees would, it is thought, enhance the effectiveness of all.

Fetal Deaths, Philadelphia, 1937-1956[*]

Year	Live Births	Fetal Deaths	Deaths/1,000 Live Births
1937	30,059	983	32.7
1941	34,118	871	25.5
1950	47,516	942	19.8
1953	51,706	932	18.0
1954	53,716	1,133	21.1
1955	52,368	1,199	22.9
1956	53,203	1,175	22.1

[*] Data from Office of Statistics and Research, Philadelphia Department of Public Health.

Even though fetal death certificates in Pennsylvania now require detailed information on pregnancy complications, and though the analysis thereof indicates the magnitude of the problem, it is to be pointed out that study committees on a community level can "individualize the cases, detect current error, and by friendly impersonal discussions can aid in producing a reduction of recurrent errors. Local problems are detected and voluntary efforts are made to correct them. Finally, the recurrent appearance of specific problems leads to laboratory and clinical research toward the solution of these at the individual, hospital, and community levels."[1]

References

1. Reishtein, W. A.: Prevention of Stillbirths, S. Clin. North America **34:**1495-1511 (Dec.) 1954.

MEDICAL NEWS

CALIFORNIA

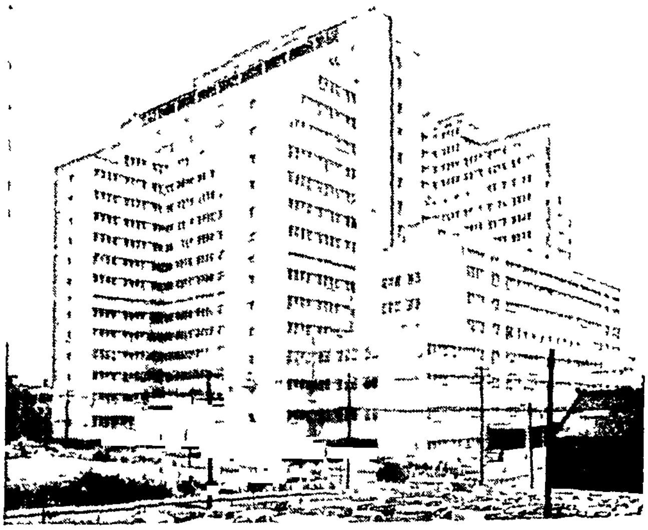
Laboratory of Neurochemistry.—A new Stanford Medical School laboratory, the Koshland Laboratory of Neurochemistry, will be established with the aid of funds from Daniel E. Koshland, president of Levi Strauss & Company, San Francisco, for basic equipment. A grant of $33,000 from the National Institute of Neurological Diseases and Blindness, U. S. Public Health Service, will help maintain the research program during its first three years. Elizabeth Roboz, Ph.D., associate professor in neurology and medical microbiology, will head the new laboratory.

Personal.—Dr. Roland A. Davison, of San Francisco, has accepted an appointment as visiting clinical professor of medicine to the Faculty of Medicine, University of Indonesia, Djakarta, Indonesia.——Dr. Arthur J. McAdams Jr. has joined the staff of Children's Hospital of the East Bay as the hospital's first full-time pathologist.——Dr. Karl M. Bowman, San Francisco, former president of the American Psychiatric Association and professor emeritus of psychiatry, University of California, during June, July, and August will be guest teacher in the Medical School of the University of Bangkok in the Orient.

GEORGIA

Dr. Bunce Receives Distinguished Service Award.—Dr. Allen H. Bunce, honorary president of the Fulton County Medical Society, Atlanta, and former president of the Medical Association of Georgia, was chosen to receive the first distinguished service award ever presented by the state association. The award, honoring Dr. Bunce was a feature of the annual session held in Macon. Dr. Bunce was secretary-treasurer of the state association for 12 years, is an honorary life member of the American Medical Association's House of Delegates, and for 10 years was a trustee of the A. M. A. He is a charter member of the World Medical Association, a trustee and president of the U. S. Pharmacopeial Convention, a member of International Pharmaceutical Federation, and a life member of the American College of Physicians.

New Grady Memorial Hospital.—Costing about 26 million dollars including equipment, the new Grady Memorial Hospital, Atlanta, is 21 stories high and covers 27.6 acres. The principal teaching hospital for Emory University School of Medicine, it has 1100 beds and 325 bassinets, 17 operating rooms, 22 emergency rooms, 19 elevators, 10 delivery rooms, and 12 x-ray rooms. The hospital was operated by the City of Atlanta from its opening in 1892 to 1945, when it became a facility of the Fulton-DeKalb Hospital Authority. It has a house staff of 110, a visiting staff of 500, paid hospital personnel numbering 1,000, and about 475 volunteer workers. The new hospital, on which construction began in March, 1954, contains Grady's first chapel, a memorial to John Newton Goddard, philanthropist. Four professional schools are maintained by the hospital: The White School of Nursing, the School of Practical Nursing, the School of Medical Technology, and the School of X-Ray Technology. The new building was dedicated in January.



The new Grady Memorial Hospital, Atlanta, Ga.

MINNESOTA

Alumni Achievement Awards.—Colonel John P. Stapp, chief, Aero Medical Laboratory, Wright Air Development Center, Dayton, Ohio, and Dr. Gordon H. Scott, dean, Wayne State University Medical School, Detroit, have received the University of Minnesota's outstanding achievement award conferred on alumni. Dr. Charles W. Mayo, of Rochester, a regent of the university, presented the awards, and Dr. Gunnar Gundersen, LaCrosse,

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Wis., president-elect of the American Medical Association, was the principal speaker. Accompanying the award to Colonel Stapp was a citation describing him as an "advocate of Air Force research in space medicine . . . physician dedicated to safer, happier lives for all mankind." Dr. Scott was cited as "builder and user of the nation's first operating electron emission microscope . . . stimulator of young men to develop their full professional capabilities."

MISSOURI

Student Winners in Beaumont Competition.—Quentin Furuya, senior at the Saint Louis University School of Medicine, has received the annual Borden award for the best original research work submitted by a senior medical student in the Beaumont Competition. Furuya, a resident of Honolulu, received a prize of $500 and a certificate of merit for his research on the influence of steroid hormones on rats with fatty livers. James B. Peter, of Omaha, Neb., received a second place award of $250 for research on the effects of insulin given to diabetic animals. Three medical seniors tied for third place awards of $75 each: Philip Higgins, St. Louis; Arthur A. Smith, Strafford, Mo.; and Raymond I. Smith, Mobile, Ala.

Dr. Wegria Named Department Head.—Dr. Rene W. E. Wegria, associate professor of medicine at Presbyterian Hospital and Columbia University College of Physicians and Surgeons, New York City, has been appointed professor of internal medicine and director of the department at the Saint Louis University School of Medicine. He will also serve as physician-in-chief of the St. Mary's Group of Hospitals. He was awarded an M.D. degree from the University of Liege in Belgium in 1936 and his doctor in medicine sciences degree (internal medicine) from Columbia University College of Physicians and Surgeons in 1945. Dr. Wegria from 1937 to 1939 was a fellow of the Belgian American Educational Foundation at Vanderbilt University, Mayo Foundation, and Western Reserve University. He joined the staff of Presbyterian Hospital and Columbia University College of Physicians and Surgeons as an assistant resident in cardiology in 1943. This year he served as visiting professor at Lovanium University in Leopoldville, Belgian Congo.

NEW JERSEY

State Medical Election.—The following officers of the Medical Society of New Jersey have been elected: president-elect, Dr. F. Clyde Bowers, Mendham; first vice-president, Dr. Jesse McCall, Newton; second vice-president, Dr. Ralph M. L. Buchanan, Phillipsburg; secretary, Dr. Marcus H. Greifinger, Newark; and treasurer, Dr. Rudolph C. Schretzmann, Hackensack.

Hospital News.—On July 18 Fitkin Hospital, Neptune, will dedicate its new air-conditioned Ford Auditorium and new wing. On July 19 a medical symposium will be held and the following speakers will participate: Drs. Murray Davidson, assistant professor of pediatrics, New York Hospital, Cornell University Medical Center, New York City; Martin L. Stone, director, department of obstetrics and gynecology, New York Medical College, New York City; Leandro M. Tocantins, professor of clinical and experimental medicine, Jefferson Medical College, Philadelphia; and Harold A. Zintel, professor of clinical surgery, Columbia University College of Physicians and Surgeons, New York City.

NEW YORK

Narcotics Research Unit in Manhattan.—A research unit in narcotic addiction will be established at Manhattan State Hospital, Governor Averell Harriman has announced. It is expected that the unit will be set up at a yearly cost of $300,000. In addition to research laboratories, examination and conference rooms, and offices, the unit will provide facilities for 30 inpatients and 150 outpatients, according to Dr. Henry Brill, assistant commissioner of mental hygiene in charge of research. Outpatients will be seen at the unit on the hospital grounds rather than at a separate aftercare clinic. Patients will be admitted on a voluntary basis only. They may be self-referred, or referred by physicians, social agencies, or courts.

New York City

Dr. Rabinowitz Goes to Chicago.—Dr. Murray Rabinowitz, of the Rockefeller Institute for Medical Research, has been appointed director of the central cardiopulmonary laboratory at the University of Chicago, effective in September, Dr. Lowell T. Coggeshall, dean of the Division of Biological Sciences including the School of Medicine, and Dr. Wright R. Adams, chairman, department of medicine, have announced. In 1952-1954 Dr. Rabinowitz was a U. S. Public Health Service fellow at Peter Bent Brigham Hospital, Boston. He also was assistant in medicine and a research fellow at Harvard Medical School. In 1955-1956 he had a U. S. P. H. research fellowship in the Institute for Enzyme Research at the University of Wisconsin, Madison. In 1957 he began working at the Rockefeller Institute for Medical Research. He recently became a diplomate of the American Board of Internal Medicine.

OHIO

Visiting Professors at Cincinnati.—The department of psychiatry, University of Cincinnati College of Medicine, has appointed visiting professors and visiting associate professors on a continuing basis: Dr. Heinz E. Lehmann will spend a number of of the **Association of Surgeons of the Southern Railway System** are: Dr. William B. Malone, II, Memphis, Tenn., president; Dr. Samuel O. Black Jr., Spartanburg, S. C., first vice-president; Dr. Max P. Rogers, High Point, N. C., second vice-president; Dr. Walter R. Brewster, New Orleans, third vice-president; Dr. Kenneth A. Morris, Jacksonville, Fla., fourth vice-president; and Dr. John M. Frere Sr., Chattanooga, Tenn., recording secretary. Mr. William J. Ashton, Box 1808, Washington 13, D. C., is secretary-treasurer.——Officers of **Western Branch, American Public Health Association,** are: president, Dr. Robert Dyar, Berkeley, Calif.; vice-presidents, Mary F. D. Chamberlain, Stockton, Calif., Dr. Edith P. Sappington, Sausalito, Calif., and Wesley O. Young, D.M.D., Boise, Idaho; and secretary-treasurer, L. Amy Darter, Berkeley, Calif.——Officers elected to serve the **American College of Allergists** from April 24, 1958, to March 19, 1959, are: president, Dr. Merle W. Moore, Portland, Ore.; president-elect, Dr. Cecil M. Kohn, Kansas City, Mo.; first vice-president, Dr. Helen C. Hayden, Chicago; second vice-president, Dr. Philip M. Gottlieb, Philadelphia; secretary, Dr. Maurice C. Harris, San Francisco; and treasurer, Dr. John D. Gillaspie, Boulder, Colo.

Wanted—Civilian Associate Editor for Armed Forces Journal.—The Department of the Navy is seeking a civilian physician for appointment as deputy director of the Armed Forces Medical Publication Agency and associate editor of its publications. Effective July 1, the professional staff of the agency will include a Medical Corps officer of one of the services as director, and a civilian deputy. Capt. Bennett F. Avery, M.C., USN, has been director of the agency and editor of its publications since July 1, 1955. Physicians interested in this new position, which will require full-time residence in Washington, D. C., should apply, prior to Aug. 1, to the Director, Armed Forces Medical Publication Agency, 2300 E Street, N.W., Washington 25, D. C. A Civil Service grade to GS-15, with a salary range to $13,970 has been established for the position. Applicants must be U. S. citizens, not over 40, and graduates of approved medical schools in the U. S. or Canada. Other requirements are a one-year accredited internship, two years of clinical experience, and five years' experience in medical editorial work. The *U. S. Armed Forces Medical Journal* has been published monthly since January, 1950, when it succeeded the *U. S. Naval Medical Bulletin,* and the *Bulletin of the U. S. Army Medical Department.*

Tenth Anniversary of World Health Assembly.—Delegates of 88 countries attending the 10th anniversary of the World Health Assembly in Minneapolis were informed May 27 that the United States was prepared to contribute to a world attack on major illnesses such as cancer and heart disease. In a message from the president of the United States read by his brother, Dr. Milton S. Eisenhower, the president described the World Health Organization as "a proven instrument through which nations and peoples of the World can combine their efforts, in friendship, toward the building of a true peace." The president's brother said that the United States would consider providing support for any sound program after investigation. Last year, he said, as a step toward coordination of research, WHO had established a close working relation with 1,800 institutions and laboratories, while 35 expert panels, with a total of 1,400 health experts, worked in many health fields. He cited the work done by WHO in developing an effective preventive vaccine against Asian influenza. He praised the success of WHO's world-wide campaign for malaria eradication. Dr. A. da Silva Travassos, director-general of health, Portugal, stated that malaria had been practically eliminated in continental Portugal and that negotiations were well advanced for a proposed regional agreement with Spain, with the aim of consolidating the eradication of the disease throughout the Iberian peninsula. Other speakers referred to various aspects of WHO activities or to plans for improving health in their respective countries. They represented Spain, Lebanon, Italy, Argentina, Jordan, Ethiopia, Union of South Africa, Cambodia, Philippines, Denmark, Iraq, Austria, Japan, Czechoslovakia, Switzerland, and Yugoslavia. Dr. M. Allaria, Ministry of Public Health and Welfare, Argentina, outlined a new plan for improving health, welfare, and social services in Argentina, explaining that his country was entering an era in which a personal and collective sense of security would be sought for all, as well as the raising of health levels of the whole population. Mr. J. Garcia Orcoyen, director-general of health, Spain, reaffirmed his country's faith in WHO. Dr. P. J. Garcia, secretary of health, Philippines, reported that his country was now feeling the full global impact of the work of the World Health Organization. Many important health projects were operating, he said, from communicable disease control to extensive training of all categories of health personnel. The Philippines is host to the WHO Regional Office for the Western Pacific, for which a new building is being constructed in Manila to be completed this year. Mr. Z. Stich, deputy minister of health for Czechoslovakia, mentioned the success that his government had obtained over the past few years in raising health standards. There is a large number of newly-trained physicians, he said and the ratio is now one doctor for 650 persons. Similar advances were being made in the field of infant mortality which decreased more than three times since 1946. He added that Czechoslovakia was eager to share this experience with the rest of the world within the framework of the World Health Organization. Six health ministers, WHO's first director-general, Dr. Brock Chisholm, of Canada, and two former presidents of the World Health Assembly, Dr. Karl Evang, of Norway, and Dr. Joseph N. Togba, of Liberia, were among the speakers at this anniversary meeting. Dr. Chisholm said that, during visits to some 20 countries in the past six months, he had witnessed how WHO had come to be recognized for its efficiency. This, he said, was due to the unique character of WHO's executive board, whose 18 members act purely as health experts and not as representatives of governments. Emphasizing that many of the difficulties that confronted WHO in its first 10 years has been overcome, Dr. Evang, director-general of Norway's Health Services, said that the organization had nevertheless been unable to use the technical knowledge at its disposal as fully as it should, due to its lack of funds. It had been hoped, 10 years ago, to establish the organization's starting budget at 25 million dollars a year to be followed by a gradual expansion over the years. This minimum had not been achieved. He said that there was a tendency, even among the most generous members, to be rather reluctant in their financial support of WHO, and at the same time, to spend larger amounts for international health work under bilateral arrangements outside WHO. Dr. Joseph N. Togba, director-general, National Public Health Service of Liberia, described the benefits his country had derived from the assistance of WHO. Yaws, a crippling disease of the topics, which 10 years ago affected between 30% and 50% of the population, now is found only in about 1%. Ten years ago there were 10 practicing physicians in Liberia; today there are 90. The 3 hospitals and clinics have increased to 20 hospitals with 60 or more clinics or health units. Today, Liberia is training its own nurses, midwives, laboratory technicians, and sanitary inspectors. The minister of public health and social welfare of Guatemala, Dr. M. Lopez Herrarte, praised the efforts made by the World Health Organization and the Pan American Sanitary Bureau, its regional office in the Americas, in coordinating health activities throughout the Americas. Among the other speakers were representatives of the USSR, France, Thailand, Iran, the United Arab Republic, Israel, Canada, China, and Australia.

The commemorative session ended at noon on May 29 and was followed immediately by the 11th annual assembly which lasted until June 13. Dr. Leroy Burney, the Surgeon General of the U. S. Public Health Service, was chosen president by unanimous vote. A budget of $14,287,600 proposed for 1959 was passed unanimously. Other important questions considered were smallpox and malaria eradication, sports medicine, and the peaceful use of atomic energy. The assembly adopted a resolution introduced by the U. S. delegation which would require a two-thirds vote to fix the budget ceiling in the future. This has been by majority vote previously.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	June 7, 1958		June 8, 1957 Total
	Paralytic Type	Total Cases	
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	1	1	..
Middle Atlantic States			
New York	3	3	..
New Jersey	..	..	1
Pennsylvania	..	..	..
East North Central States			
Ohio	..	..	..
Indiana	..	..	..
Illinois	..	1	1
Michigan	1	1	..
Wisconsin	..	..	..
West North Central States			
Minnesota	..	..	..
Iowa	1	1	..
Missouri	..	..	1
North Dakota	..	..	..
South Dakota	..	..	2
Nebraska	..	1	..
Kansas	..	..	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	1	1	1
West Virginia	..	1	1
North Carolina	..	1	2
South Carolina	1	1	3
Georgia	..	..	..
Florida	..	..	5
East South Central States			
Kentucky	..	..	..
Tennessee	..	..	1
Alabama	..	1	2
Mississippi	..	1	3
West South Central States			
Arkansas	1	1	..
Louisiana	1	1	5
Oklahoma	..	1	4
Texas	2	9	20
Mountain States			
Montana	..	..	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	2
New Mexico	..	..	2
Arizona	..	..	1
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	..	..
Oregon	..	..	1
California	2	3	15
Territories and Possessions			
Alaska	..	..	..
Hawaii	1	1	..
Puerto Rico	2	2	1
Total	17	32	74

meet the present and future needs of the Army. He will serve as principal advisor to the surgeon general and to the chief of the research and development division in the surgeon general's office on all scientific and technical matters concerning research and development.

Dr. Youmans is now serving as consultant to the Army surgeon general's preventive medicine division; as consultant to the interdepartmental committee on nutrition for national defense; member, Assistant Secretary of Defense Panel on Military Medicine; and as member, National Research Council Committee for the Quartermaster Subcommittee on Nutrition.

A retired Army Medical Corps colonel, Dr. Youmans served in China, the Pacific, and the European Theaters in World War II, and was awarded the Legion of Merit and the French Legion of Honor. During World War II he was also in charge of the nutrition division in the surgeon general's office. Dr. Youmans, who will be 65 years old in September, has served as dean and professor of medicine at Vanderbilt University since 1950. Born in Wisconsin, Dr. Youmans received his doctor of medicine degree at Johns Hopkins University in 1919. He is the author of many scientific papers and three books.

NAVY

Meeting of Reserve Consultant Board.—A group of civilian physicians met at the Naval Medical Center, Bethesda, Md., on May 23, to discuss the Navy's graduate medical training program with the surgeon general and his staff. Each member of the Board represented one of the medical specialties, and the majority of them hold teaching positions at medical schools throughout the United States.

The Navy's graduate medical training program was instituted at the close of World War II by several of the members of the Board who were in the naval reserve, on active duty at that time. Since release from active duty they have continued their interest and have given of their time and advice, visiting the Navy's medical facilities at the request of the surgeon general, to review the training programs. The program is said to be a very important feature of the professional career pattern of the Navy.

Personal.—Edward L. Alpen, Ph.D., head of Biophysics Branch, Naval Radiological Defense Laboratory, San Francisco, has been awarded a one-year National Science Foundation Senior Postdoctoral Fellowship at the Radiobiology Institute of United Oxford Hospitals, Oxford University, England. He will work in the radiotherapy department of Churchill Hospital on the effects of radiation on blood cell life span. He will also spend a month at the Centre National de Transfusion Sanguine, Paris, France. Dr. Alpen will leave San Francisco early in August.

PUBLIC HEALTH SERVICE

Referral of Patients to National Institutes.—For physicians who may be interested in referring certain patients for study to the Clinical Center of the National Institutes of Health, Bethesda, Md., the following information is provided concerning diagnoses that are of particular current interest. This list supplements a more extensive compilation published each year in booklet form.

Letters of referral should include an adequate history and may be addressed to the director of the clinical center for registration and circulation among appropriate clinical groups. A full report of findings will be furnished the referring physician when an accepted patient is discharged back to his care.

The National Cancer Institute has particular interest in patients with the following diagnoses: acute leukemia, any age; Hodgkin's disease without previous therapy; multiple basal cell cancers of the skin; myeloid metaplasia; protein disturbances such as macroglobulinemia, cryoglobulinemia, and idiopathic hypoalbuminemia; cancer of any type in children; choriocarcinoma.

As candidates for radiologic study and treatment patients in the following categories will be considered: invasive carcinoma of the urinary bladder without bony or extrapelvic metastases and without previous external radiation therapy or extravesical surgery; squamous cell carcinoma of the oropharyngeal and laryngeal cavities; carcinoma of the esophagus without evidence of metastases to neck or liver; carcinoma of thyroid; solitary myeloma; chondrosarcoma.

The Allergy and Infectious Diseases Institute has especial current interest in proved or strongly suspected cases of disseminated histoplasmosis. Studies include improved diagnostic methods, new therapeutic agents, and basic immunology.

The National Heart Institute has particular need for patients with hormone-producing malignancies of the adrenal gland for trial of Δ^4 cholestenone, which is an inhibitor of adrenal steroid synthesis. Patients with postoperative recurrences of adrenal malignancy are also considered suitable for trial.

Other conditions of interest to Heart Institute investigators include: malignant hypertension, primary pulmonary hypertension, and cases which though sustained have had no serious cardiac, renal, or cerebral complications; angina pectoris clearly associated with coronary artery disease; pheochromocytomes; and adrenogenital syndrome.

DEATHS

Alberton, Edmond C. ⊕ San Francisco; University of California School of Medicine, San Francisco, 1941; specialist certified by the American Board of Internal Medicine; member of the American College of Chest Physicians; veteran of World War II; on the staff of the Mount Zion Hospital; died April 19, aged 41, of coronary thrombosis and hypertension.

Algire, Glenn Horner ⊕ Senior Surgeon, U. S. Public Health Service, Bethesda, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1940; member of the American Society for Experimental Pathology; service member of the American Medical Association; associated with the Clinical Center, National Institutes of Health; died in the Walter Reed Army Hospital in Washington, D. C., April 28, aged 50.

Alter, Joseph Galbraith, New Kensington, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1895; died April 24, aged 85.

Anderson, Axcel Engelbert ⊕ Fresno, Calif.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; fellow of the American College of Surgeons; past-president of the Fresno County Medical Society; on the staffs of St. Agnes and Fresno Community hospitals; died in Pasadena April 11, aged 81, of cerebral thrombosis.

Backenstoe, Martin John, Emmaus, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1890; an associate member of the American Medical Association; the founder and organizer of the Emmaus National Bank, serving as its president for 14 years; later became founder, president, and board chairman of Security Trust Company; director of the Second National Bank in Allentown; past-president of the Luzerne County Medical Society; trustee of the Moravian College for Women in Bethlehem; died in the Sacred Heart Hospital, Allentown, April 26, aged 90, of arteriosclerosis.

Baggs, Albert Nicholas ⊕ Washington, D. C.; University of Pennsylvania Department of Medicine, Philadelphia, 1892; veteran of World War I; during World War II associated with the Selective Service System; at one time served with the Veterans Administration; died May 1, aged 87.

Balliet, Calvin Joseph ⊕ Lehighton, Pa.; Jefferson Medical College of Philadelphia, 1897; died in the Gnaden Huetten Memorial Hospital April 29, aged 83.

Bass, William Johnson, Paducah, Ky.; University of Louisville (Ky.) Medical Department, 1892; served as city physician and as county coroner; on the staffs of the Illinois Central Railroad and Riverside hospitals; died in the Western Baptist Hospital April 22, aged 89, of multiple small cerebral vascular accidents.

Bell, John Bethel, Milan, Tenn.; Meharry Medical College, Nashville, 1924; died in Memphis April 13, aged 68, of coronary occlusion, embolus and thrombosis.

Besemer, Arthur, Cupertino, Calif.; Cleveland Medical College, Homeopathic, 1892; an associate member of the American Medical Association; member of the American Academy of General Practice; veteran of World War I; for many years practiced in Marion, N. Y., where he was town health officer and county coroner; died in Sunnyvale April 18, aged 93, of cerebral thrombosis.

Billingsley, Gordon David, Los Altos, Calif.; University of Oregon Medical School, Portland, 1929; on the staff of the Palo Alto Hospital; veteran of World War II; died April 27, aged 55, of coronary thrombosis.

Black, William Thomas, Quitman, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1910; member of the Texas Medical Association; served as county health officer; died April 30, aged 80, of cerebral hemorrhage.

Booth, Donald S. ⊕ Toledo, Ohio; University of Michigan Medical School, Ann Arbor, 1928; for many years associated with the Mercy Hospital; died April 30, aged 55, of coronary occlusion.

Brayman, Charles W. ⊕ Cedar Springs, Mich.; Grand Rapids Medical College, 1902; charter member of the Cedar Springs Rotary Club, serving as its first secretary and later president; died in the Butterworth Hospital, Grand Rapids, April 30, aged 86.

Brown, Edwin N., Arena, Wis.; Northwestern University Medical School, Chicago, 1902; associated with the Methodist Hospital in Madison, where he died April 12, aged 82, of heart disease.

⊕ Indicates Member of the American Medical Association.

Kelly, Thomas Charles, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1904; formerly assistant professor of pediatrics at his alma mater and University of Pennsylvania Graduate School of Medicine; specialist certified by the American Board of Internal Medicine; member of the American Academy of Pediatrics and the American Clinical and Climatological Association; an associate member of the American Medical Association; fellow of the American College of Physicians; veteran of World War I; on the honorary staff of Fitzgerald Mercy Hospital in Darby and St. Christopher Hospital for Children and Misericordia Hospital, where he died April 22, aged 75, of arteriosclerotic heart disease.

Kleckner, Martin Seler ⊕ Allentown, Pa.; born in Allentown April 14, 1890; University of Pennsylvania School of Medicine, Philadelphia, 1914; specialist certified by the American Board of Surgery and the American Board of Proctology; member and past-president of the American Proctologic Society; fellow of the International College of Surgeons and American College of Surgeons; chairman, Section on Gastroenterology and Proctology of the American Medical Association, 1947-1948; director of the Pennsylvania Division of the American Cancer Society; served as president of the cancer unit of Lehigh County; past-president of the Lehigh County Medical Society; on the staffs of St. Luke's Hospital in Bethlehem and Sacred Heart Hospital; chief of the proctology department, Allentown Hospital, where he died May 1, aged 68, of pulmonary edema.

Knight, John Augusta ⊕ Beaumont, Texas; Memphis (Tenn.) Hospital Medical College, 1904; associated with Hotel Dieu Hospital; died in Columbus, Ga., April 21, aged 76, of uremia.

Kohlbraker, George Henry, Norristown, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1919; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; for many years on the staff of the Norristown State Hospital; served as clinical director of the Danville State Hospital in Danville, Pa.; died April 27, aged 63.

Leatherwood, Elbert Fountain ⊕ Hayneville, Ala.; University of Alabama School of Medicine, Mobile, 1907; served as health officer for Lowndes County and as part-time health officer of Butler County; for many years councillor of the Second District of the Medical Association of the State of Alabama; died April 18, aged 78, of arteriosclerosis.

Levy, Jesse Goldberg ⊕ Buffalo; University of Buffalo School of Medicine, 1906; died April 21, aged 75.

Lewis, John Francis, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1912; service member of the American Medical Association; veteran of World War I; for many years chief medical officer of the Veterans Administration; died in the Misericordia Hospital April 22, aged 71.

Lexa, Frank Joseph ⊕ Lonsdale, Minn.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; died April 11, aged 75.

Lyons, Andrew James, Highland Park, Ill.; Chicago College of Medicine and Surgery, 1916; veteran of World War I; for many years on the staff of the Veterans Administration Hospital in Hines; died in the U. S. Naval Hospital in Great Lakes May 11, aged 83, of abdominal cancer.

McConkey, Mack, Saranac Lake, N. Y.; Harvard Medical School, Boston, 1925; member of the American Trudeau Society and the American Clinical and Climatological Association; member of the staff of the Ray Brook (N. Y.) State Hospital; veteran of World War I; died April 14, aged 64, of tuberculosis.

McLeod, James Newton ⊕ Dallas, Texas; University of Texas School of Medicine, Galveston, 1920; fellow of the American College of Surgeons; served on the staffs of the Parkland Hospital and St. Paul's Hospital, where he died April 23, aged 68, of coronary disease.

McWhorter, William Breese ⊕ Anderson, S. C.; Emory University School of Medicine, Atlanta, 1915; fellow of the American College of Surgeons; on the staff of the Anderson Memorial Hospital, where he died April 15, aged 65, of chordoma in the sacral region.

Manovill, Edwin Godfrey, Jackson Heights, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1926; served on the faculty of his alma mater; associated with the Physicians Hospital in Jackson Heights and the Roosevelt Hospital in New York City; died May 3, aged 55, of coronary thrombosis.

Malloy, Ellsworth Francis ⊕ Fremont, Neb.; Creighton University School of Medicine, Omaha, 1928; associated with the Dodge County Community Hospital, where he died April 15, aged 59, of myocardial infarction.

Miller, Edward Walter Jr., Carmel, N. Y.; University of Louisville (Ky.) School of Medicine, 1948; interned at New Rochelle (N. Y.) Hospital; served a residency at the Hartford (Conn.) Hospital and the Norwich (Conn.) State Hospital; died in Stockton, Calif., April 19, aged 35.

Moorhead, Stirling Walker ✠ Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1905; formerly on the staff of his alma mater; specialist certified by the American Board of Urology; member of the American Urological Association; founding member and past-president of the Philadelphia Urological Society; served as member and president of the staff, Methodist Hospital, and on the staff of the Hospital of the University of Pennsylvania; member of the staff of the Fitzgerald Mercy Hospital in Darby, where he died April 26,. aged 76, of generalized carcinomatosis.

Murphy, James Howard ✠ Des Moines, Iowa; Creighton University School of Medicine, Omaha, 1930; veteran of World War II; on the staff of the Mercy Hospital, where he died April 15, aged 51, of carcinoma of the stomach.

Neuberger, Joseph Anton, Cleveland; University of Wooster Medical Department, Cleveland, 1908; died in the Lakeside Hospital April 21, aged 81, of arteriosclerotic heart disease.

Penrose, James Brinton, Marietta, Ohio; University of Pennsylvania Department of Medicine, Philadelphia, 1906; member of the Ohio State Medical Association; past-president of the Washington County Medical Society; died in the Marietta Memorial Hospital April 11, aged 76, of cerebral hemorrhage.

Petillo, Diomede, New York City; Regia Universita di Napoli Facolta di Medicina e Chirurgia, Italy, 1907; consulting urologist at Italian Hospital; died March 25, aged 77, of cancer of the lung.

Ralston, Robert Linton ✠ Spartanburg, S. C.; Georgetown University School of Medicine, Washington, D. C., 1945; specialist certified by the American Board of Otolaryngology; lieutenant (jg) M. C., U. S. Naval Reserve from 1946 to 1948; on the staff of the Spartanburg General Hospital; died suddenly April 26, aged 38, of acute coronary occlusion.

Rodman, John Stewart, Radnor, Pa.; born in Abilene, Texas, July 2, 1883; Medico-Chirurgical College of Philadelphia, 1906; emeritus professor of surgery at Woman's Medical College of Pennsylvania, Philadelphia; member of the founders group and formerly secretary of the American Board of Surgery; medical secretary of the National Board of Medical Examiners; served as president of the Philadelphia Academy of Surgery and vice-president of the American Surgical Association; fellow of the American College of Surgeons; an associate member of the American Medical Association; veteran of World War I; associated with the Hospital of the Woman's Medical College of Pennsylvania, Bryn Mawr, (Pa.) and Presbyterian hospitals; died April 26, aged 74, of left hemiplegia and coronary occlusion.

Ruml, Wentzle ✠ Cedar Rapids, Iowa; Northwestern University Medical School, Chicago, 1891; for many years president of the school board; associated with St. Luke's Hospital; died April 18, aged 90.

Ruttenberg, Lewis Harris, Lincolnwood, Ill.; Milwaukee Medical College, 1912; served as medical examiner for the Chicago Rapid Transit Company and later the Chicago Transit Authority; died May 11, aged 74.

Schneider, William John ✠ Homeland, Ga.; John A. Creighton Medical College, Omaha, 1910; for many years mayor; died in Folkston April 17, aged 74, of a heart attack.

Scheppler, George Carol ✠ Blue Lake, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1945; member of the American Academy of General Practice; medical health director at Humboldt State College in Arcata; associated with General and St. Joseph hospitals in Eureka and the Trinity Hospital in Arcata; died in Arcata April 18, aged 41, of injuries received in an automobile accident.

Steele, Noah Edward, Logan, W. Va.; University of Louisville (Ky.) Medical Department, 1913; veteran of World War I; president of the Valley Realty Company; died in Huntington April 18, aged 70, of uremia.

Steele, William Edward ✠ Seattle; Hahnemann Medical College of the Pacific, San Francisco, 1913; member of the Industrial Medical Association; veteran of World War I; formerly chief medical adviser to the state department of labor and industries; served as medical director of the Bethlehem Pacific Coast Steel Corporation; died in the Virginia Mason Hospital April 17, aged 72, of cerebral thrombosis.

Terwilliger, William Clarence, Akron, Ohio; Chicago College of Medicine and Surgery, 1915; member of the Ohio State Medical Association; died in the Cleveland Clinic Hospital April 11, aged 71.

FOREIGN LETTERS

DENMARK

Operations on the Aged.—Dr. H. Faber (*Nordisk medicin*, May 15, 1958) reviewed his experiences with two series of patients, over the age of 70, admitted to hospital in the periods 1947 to 1951 and 1952 to 1956 respectively. The operation rate increased in the second period, as determined to a great extent by the rise in the number of major operations. The two series were not strictly comparable in that several of the patients admitted to hospital and operated on in the second period might not even have reached the hospital in the earlier period. Of the 101 patients in the second period who were not operated on, operation was recommended for 13, but they refused. A common contraindication was cerebral arteriosclerosis associated with disease of the kidneys, heart, and blood vessels. The mean age of the patients with prostatic hypertrophy was much the same (76 and 75 years respectively) for the patients operated on or not. In patients with marked senile dementia operative treatment was withheld except on the rare occasions when it was required for reasons of nursing. Faber often found that even severe psychic disturbances yielded to the restoration of a normal somatic balance. He also noted that many of the recent advances in surgery were first applied to the aged, for whom early ambulation and reduction of anesthesia to the minimal dosage and duration were found necessary.

Lumbago-Sciatica.—Dr. S. Staffeldt (*Nordisk medicin*, May 8, 1958) studied two series of 100 patients with lumbago-sciatica to evaluate the comparative merits of active and passive treatment. His first series, treated at the same hospital, consisted of the patients treated conservatively between 1938 and 1942, with strict immobilization in bed for about six weeks, thermotherapy, and massage without exercises. His second series consisted of the patients treated actively between 1949 and 1951, with early mobilization and gymnastic exercises. The criteria by which these series were judged were the duration of hospital treatment, the time taken to convert a positive to a negative Lasègue sign, and the duration of pain at rest or on movement. For patients under active treatment the stay in hospital was shortened by about 20 days. Lasègue's sign became negative sooner, and pain at rest or on movement ceased sooner. Although this comparison was favorable to active treatment the author admitted that his two series were not strictly comparable in that the records of the older series did not clearly show how many of the patients suffered from definite herniation of the nucleus pulposus. He believes that, after eliminating the 5% requiring operative relief for their symptoms, the remaining 95% need a more imaginative approach than they have hitherto enjoyed.

The Placing of Advertisements in Medical Journals.—*Ugeskrift for læger* being the organ of the Danish Medical Association, its members take a keen and proprietary interest in it, giving its editor from time to time the benefit of advice on how to run it. One reader tells how he recently went early to bed to enjoy a good cigar and to browse on the latest issue of *Ugeskrift*. From cover to cover he found his attention to the medical reading matter being constantly diverted by advertisements. He has all he needs of them in the mail, but, since the journal is in financial need of them, he suggests either that they be placed before and after the medical articles or that they be tucked between the pages which in his opinion are most read by Denmark's physicians, the pages announcing vacant medical appointments.

Deaths in 1957.—For many years the annual death rate in Denmark has been stable, with about 39,000 deaths every year. In 1957 this figure jumped to nearly 42,000, a rise of 5.5% on the figure for the preceding year. This rise was chiefly accounted for by the population over the age of 65, but all the other age groups, with the exception of infants, had their share in the rise. This must largely be attributed to the two waves of influenza, the first of which accounted for about 400 deaths (though only 60 of them were reported as influenza deaths) and the last for about 900 deaths. About 67% of all deaths in the last quarter of the year were directly or indirectly traceable to influenza. The 191 deaths from pulmonary tuberculosis were only one quarter of the number of deaths from bronchial cancer.

Activation of Articular Tuberculosis by Corticoid Treatment.—Though much has already been written about activation of pulmonary tuberculosis by cortisone or ACTH, little has hitherto been reported on the effect of this treatment on latent tuberculosis of the joints and tendon sheaths. Dr. K. S. Jörgensen (*Ugeskrift for læger*, May 15, 1958), who ob-

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served four such patients, pointed out that in only one was there a previous history of pulmonary tuberculosis. In two the knee was the site of tuberculosis, in one the forefoot, and in one the synovial flexor tendon sheath of the hand. In none of the four was latent tuberculosis suspected, the local injections of hydrocortisone being given on the assumption that the lesions were not tuberculous. As soon as the mistake was discovered, specific antituberculosis treatment was instituted. To avoid a repetition of this mistake, Jörgensen recommended a thorough clinical examination of every candidate for local injections of hydrocortisone with a roentgenogram of the joint involved and, if need be, of the lungs also. When injections provoke abnormal reactions, x-ray examinations should be repeated, supplemented if need be by an exploratory joint biopsy.

Chronic Bronchitis.—Dr. P. J. Dragsted (*Ugeskrift for læger,* May 15, 1958) reported a series of 131 patients with chronic bronchitis kept under close observation and bacteriological control for four years. In about 33% of them the bronchitis was complicated by bronchiectasis. The monthly bacteriological examinations often yielded pathogenic organisms, prominent among which were pneumococci, Hemophilus organisms, and hemolytic streptococci. Sensitivity determinations on washed sputums were performed as a guide to antibiotic treatment, and, in addition to a sulfonamide, trial was made with penicillin in 40 patients, chloramphenicol in 26, and chlortetracycline in 17. The dosage was large because of the chronicity of these cases. Good correlation was established in respect of the treatment given patients presenting pneumococci and Hemophilus organisms, but not as regards hemolytic streptococci. Dragsted believes that the treatment he outlines can do much to reduce the chronic invalidism to which these patients are subject.

FINLAND

Prognosis of Myocardial Infarction.—E. Iisalo and co-workers (*Nord. Med.* 59:264, 1958) conducted a follow-up study of 370 patients who had been hospitalized for acute myocardial infarction and re-examined six months to five years after their discharge. They found that 87 (23.5%) had died. Another 51 could not be located. Of the remaining 242 patients 10.7% had no subjective symptoms, 75.6% had angina pectoris as the main prevailing subjective symptom, and 26.9% had symptoms of cardiac insufficiency which were objectively confirmed. Sixty-eight patients (28.1%) had been readmitted for recurrent myocardial infarction or other cardiac diseases. The digitalis therapy after discharge was found to be unsatisfactory in many of the patients with cardiac insufficiency. This points to a need for more effective supervision during the convalescent period and later. In this series 60.7% of the patients had recovered sufficiently to resume their former occupations; 9.1% began working one month, 33.9% three months, and 53.7% six months after discharge. The proportion who were unable to resume their former occupations was 39.3%. Coronary insufficiency was the main reason in two-thirds of these patients. Two-thirds of the patients whose electrocardiograms revealed persistent auricular fibrillation or flutter and the same proportion of those with a permanent QS pattern in unipolar chest leads considered themselves capable of working. Two-thirds of those whose electrocardiograms had become normal by the time of the follow-up examination were at work. With certain exceptions, electrocardiographic changes were not reliable criteria for evaluating the ability of patients with acute myocardial infarction to resume work later. The later course of the disease was found to conform largely with the early prognosis. This was indicated by the number of those who had recovered and were symptom-free, by the rate at which they resumed their former occupations, by the number who were readmitted for treatment, by the number that remained incapacitated, and by the mortality.

Goiter and Thyrotoxicosis.—Dr. E. Saarenmaa (*Duodecim* 3:131, 1958) stated that, although the views of internists and surgeons on the treatment of goiter and thyrotoxicosis may disagree, it should be possible to find a common ground. The treatment of goiter may also differ with the geographic location. Although statutory goiter prophylaxis is good, newspaper propaganda exaggerates its importance. In addition, iodine prophylaxis is widely available—various deep sea products can be bought even in remote villages, and livestock are fed with iodine-containing foods. Colloid goiter is the result not only of an exogenous factor but also of an endogenous individual factor: the inability to utilize the iodine in the food. The basic elements of the thyroid gland are epithelium, colloid, and stroma. Accordingly a goiter can be defined as normoepithelial, hypoepithelial, or hyperepithelial. Endemic goiter in Finland is of the hypoepithelial type, and indications for its treatment are pressure symptoms and cosmetic disfigurement. In the case of very young persons these factors usually do not justify surgical or other active treatment, with the possible exception of thyroid hormone. Inorganic iodine can probably cause epithelial proliferation in an iodine-deficient gland with the endemic type of goiter, after which toxic symptoms appear. More important than the therapeutic problem of endemic goiter is that of hyperepithelial goiter with thyrotoxicosis. The three forms of radical therapy include surgery, antithyroid preparations combined with iodine, and radioactive iodine. Surgery is the

FOREIGN LETTERS

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ment, which returned to normal in spite of the continuation of treatment. The blood urea and nonprotein nitrogen levels did not show any marked rise during treatment and fell with improvement in the patient's general condition. The serum cholesterol concentration showed a definite decline. The most remarkable improvement was in the serum proteins, the serum albumin concentration showing a rise as treatment was continued and returning to normal limits within two or three months of the initiation of treatment. These levels remained normal even in the three patients who continued to pass traces of albumin in the urine. All the patients were in remission after follow-up periods in some cases of over two years.

Amebiasis.—Roy Chowdhary and co-workers (*J. Indian M. A.* 30:8 [April 16] 1958) used two new preparations, 11'925 and 11'925C, chemically unrelated to any of the known amebicidal drugs, to treat 70 patients with acute and chronic amebiasis. The first is a semicarbazone of 5,6-quinone-4,7-phenanthroline and is available in 100-mg. tablets. Its lowest amebicidal concentration in vitro is 1:8,000 which is comparable to that of iodochlorhydroxyquin, carbarsone, and chlortetracycline. The second compound is also a 5,6-quinone-4,7-phenanthroline and is available in 50-mg. tablets. Good amebicidal action in vitro was obtained with a concentration of 1:16,000. The in vivo action was tested in rats, and both drugs were found to have a low general toxicity. All the 70 patients selected for clinical trial had either cystic or vegetative forms of Entamoeba histolytica in their stools except five who had a past history of amebiasis. The first drug was tried in 21 cases, the second in 40, and 9 were given both. The former was usually given in a daily dosage of 600 mg. in acute cases and 300 mg. in chronic cases. The dosage of 11'925C varied from 300 to 500 mg. daily.

Of the 21 patients treated with 11'925, 6 had acute and 9 had chronic dysentery, and in 6 there was an associated hepatitis. Vegetative forms of E. histolytica were present in the stools of five of the six patients with acute dysentery. With a dosage of 600 mg. daily for six to nine days, the vegetative forms of the parasite disappeared in three within a week, but cystic forms persisted in two. Clinical cure was obtained in two, symptomatic relief in two, slight amelioration in one, and no relief in one. Of the nine with chronic dysentery passing amebic cysts in their stools, the cysts disappeared after treatment in eight. Clinical cure was obtained in six, moderate relief in one, and no relief in two. Of the 6 patients who had a complicating hepatitis, one had acute and five had chronic dysentery. All had amebic cysts in their stools, which disappeared after treatment. Cure was achieved in four, symptomatic relief in one, and one did not respond. Tenderness and the enlargement of the liver began to diminish in five within a week. Of these 21 patients, 18 had nausea and vomiting between the first and fourth days of treatment.

The second drug was used on 40 patients, 7 with acute dysentery, 22 with chronic dysentery, and 11 with an associated hepatitis. Vegetative forms of the parasite were present in two and cystic forms in five patients with acute dysentery. The stools became negative and clinical cure was obtained in all patients. One patient with acute dysentery had a Salmonella infection with a past history of amebiasis. He also responded to the drug. Of the 22 with chronic dysentery, one passed vegetative forms, 17 passed amebic cysts, and in 4 the diagnosis was based on history and symptoms. Stools became negative in all but one, who continued to pass cysts. Clinical cure was obtained in 16, symptomatic relief in 1, and the others obtained partial or no relief. Of the 11 with hepatitis, 2 had acute and 9 chronic dysentery. All had cysts in their stools, and those with acute dysentery also passed the vegetative forms. Cure was obtained in seven, symptomatic relief in one, and moderate relief in three. In all but one, the tenderness and enlargement of the liver diminished in 7 to 10 days.

In the group that received combined treatment, initial trial with 11'925 had to be given up due to the appearance of intractable nausea and vomiting; the treatment was therefore continued with 11'925C. This group contained four with acute and five with chronic dysentery. One had vegetative forms of the parasite, and eight had cysts in their stools. After treatment the vegetative forms disappeared, but the cysts persisted in two. Clinical cure was obtained in five, symptomatic relief in two, and moderate relief in two. The side-effects of nausea and vomiting noticed with 11'925 disappeared at once when 11'925C was given, and clinical improvement was observed, but with the latter drug highly colored urine appeared in four patients. Thus, about 75% of the patients responded favorably to 11'925 within 7 to 10 days, the rest not showing improvement mainly due to the drug-induced nausea and vomiting. With 11'925C, 95% were relieved immediately within 7 to 10 days. Hepatic manifestations also improved with both drugs. The combined treatment further showed the nontoxic nature of the latter drug and its efficacy.

Leprosy.—The chairman of the Indian Leprosy Association announced that the success of sulfone treatment had stimulated mass leprosy treatment campaigns in all countries where leprosy was endemic. The most hopeful feature of these campaigns seemed to be that gradually a large number of patients with early leprosy were presenting themselves for treatment and that each year a large

CORRESPONDENCE

SAFFLOWER OIL AND PLASMA CHOLESTEROL

To the Editor:—A paper by Perkins, Wright, and Gatje in the April 26, 1958, issue of THE JOURNAL, page 2132, presents data which indicate that the addition of safflower oil to an average American diet produces no depression of plasma cholesterol level. The authors estimated that the final ratio of unsaturated to saturated fat in the diet was about one to two. The absolute amount of safflower oil was slightly less than 50 Gm. The safflower emulsion was added without any reduction in the diet calories, i.e., the total caloric intake was increased by something more than 400 calories per day.

This paper is timely, inasmuch as one cannot overemphasize the fact that, if lowering of the plasma cholesterol level is to be achieved by the use of polyunsaturated fats, it is necessary to modify the entire diet. This is brought out to some degree in a recent paper by my associates and me in *The Lancet* (2:334 [Feb. 15] 1958), in which approximately 50% of dietary saturated fat was substituted by unsaturated fat before a significant lowering of plasma cholesterol level occurred.

In ambulatory studies in patients with known atherosclerosis, we have frequently found that it is necessary for a time to completely replace all saturated fat in the diet by unsaturated fat and also to replace a considerable portion of the concentrated carbohydrate by unsaturated fats, in order to achieve the initial lowering. Once such an effect has been produced, it is frequently possible to liberalize the diet by gradual inclusion of increasing amounts of saturated fat. The speed with which this may be done is a highly individual matter. As in the case of management of the diabetic, there is no single dietary program which is applicable to all patients with a given type of problems.

Perkins and associates state: "Our results are not to be construed as denying the possible effectiveness of safflower oil as a supplement to diets which have been markedly reduced in their content of animal fat." It may be well to emphasize this particular paragraph, and to further emphasize that when polyunsaturated fats in the form of safflower oil or other highly unsaturated fats are used in a proper fashion, a highly predictable and significant lowering of levels of cholesterol and other plasma lipids will result.

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RADIATION HAZARDS

To the Editor:—In behalf of the Health Resources Advisory Committee of the Office of Defense Mobilization, I want to compliment THE JOURNAL on the excellent editorial on Radiation Hazards and Radiation Syndrome that appeared in the May 10th issue (page 220). This is a subject on which every practicing physician should be informed, both in order to deal with the clinical problems which result from the increasing use of radiation today and in order to prepare himself to render effective service in a national emergency.

The levels of radiation exposure which could result from fall-out after nuclear explosions far exceed those that are encountered in ordinary practice even in high intensity radiotherapy. Experience with the acute radiation syndrome as presented by patients undergoing therapy is largely limited to radiologists.

Dr. Gerstner's excellent article on Acute Radiation Syndrome in Man (U. S. *Armed Forces M. J.* 9:313 [March] 1958) which is so admirably summarized in the editorial, presents in readable form information and analysis which should be in the hands of every physician in the United States. The Health Resources Advisory Committee commends this subject for the serious consideration of the entire medical profession.

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PROTAMINE SULFATE AND HYPERHEPARINEMIA

To the Editor:—In a recent report of the Council on Drugs in THE JOURNAL of May 3, 1958, page 64, on protamine sulfate, N. F., no mention was made of the ineffectiveness of this agent in idiopathic or congenital hyperheparinemia. In a study of a patient with this condition (*Am. J. M. Sc.* 234:251-258 [Sept.] 1957), Miss Hussey and I found that the intravenous injection of 50 mg. protamine sulfate actually increased the heparin titer and further prolonged the clotting time. It appears that protamine sulfate stimulates the output of heparin in the blood of this patient. In the test tube, on the contrary, the heparin in this patient's blood is neutralized either by protamine sulfate or toluidine blue as determined by the thrombin time test described in my monograph (Hemorrhagic Diseases, Philadelphia, Lea & Febiger, 1957, page 431).

During the two and a half years that his patient has been repeatedly studied, the clotting time has usually been over 40 minutes. At present, her blood is totally incoagulable. This is probably the result of her pregnancy. After the birth of her first two babies, she required 34 and 30 transfusions, respectively, to control the postpartum hemorrhage. Interestingly, she has had no spontaneous hemorrhages, her menses have always been normal, and she does not bruise easily. Even now, when her blood will not clot in a test tube kept at 37° C., only one small ecchymotic spot was found in a recent physical examination.

In view of the observation that despite a persistently pronounced hyperheparinemia, a patient may manifest no bleeding tendency except after rather severe trauma, one should be cautious against attributing a hemorrhagic state to an increase of heparin in circulation, especially when determined by as indefinite a procedure as the protamine titration test. Attention should also be called to the striking lack of correlation between the clotting time and defective hemostasis

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SERIAL CHOLECYSTOGRAPHY

To the Editor:—The review (*J. A. M. A.* 166:1897-1898 [April 12] 1958) of the article on serial cholecystography, by Rose, from the *British Medical Journal* (1:360-362 [Feb. 15] 1958) should bring protests. If cholecystectomy were to be based on the ability of the gallbladder to contract after the administration of certain cholagogues, then certainly the population of the world would be inflicted with surgical scars in the right upper quadrant. The postcholagogue film in good cholecystography is merely to occasionally uncover abnormality in the gallbladder not suspected on the conventional precholagogue film. Actually the postcholagogue examination in cholecystography is of most value in demonstrating the condition of the cystic and common ducts. In recent years in approximately 35 to 40% of examinations some portion of the biliary tree is visualized in addition to the gallbladder by this method.

In these days of increased consciousness of irradiation hazard from diagnostic radiology, any method which proposes 8 or 10 films for a single examination must be viewed with concern. In well-controlled diagnostic radiology under the direction of a qualified radiologist, the average total number of films should rarely exceed two per examination. This can be attained only by use of the lateral decubitus position in radiography of the gallbladder.

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IRON ABSORPTION

To the Editor:—In an editorial in the April 5, 1958, issue of The Journal, page 1742, the statement is made that "the taking of iron with a meal reduces iron absorption by about 50%." Interference of iron absorption by food solids may be much greater than this. Sharpe and others (*J. Nutrition* 41:433-446 [July 10] 1950) noted 20% as much absorption of iron (Fe^{55}) from the breakfast meals of 17 boys as from water meals. This calculation was based on hemoglobin formation.

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THE LEISURE CORNER

FUN ON A BICYCLE

Not since the turn of the century have Americans been as interested in the bicycle as they are now. Today more than 18 million bicycle riders are on the road. The automobile dominated the scene during the first half of the 20th century, and bicycling was left to racers, faddists, youngsters, and those old-timers who never seemed to get over their first love for the bicycle. With the popularization of the automobile moving the legs around in self-propulsion was considered passé; in fact, in 1933, many bicycle manufacturers were forced out of business as their production dropped to a new low.

Millions of Americans have awakened to the pleasures associated with riding a bicycle. The bicycle permits them to visit picturesque out-of-the-way places the automobile cannot reach. Here, the smell of fresh country air is uncontaminated by exhaust fumes. Coasting down a hill on a bicycle, wind whistling past one's ears, leaves unforgettable memories. Bicycling provides exercise for some people, a means of reducing for others, and a source of recreation for everyone. Compared to other means of transportation that are completely dependent on the expenditure of physical energy, the bicycle is a most efficient type of vehicle. It occupies little space, requires a minimum amount of care, and has a long life. More and more women use bicycles for marketing, and it is interesting to note how much better health many of them enjoy.

Many beginners who are introduced to the bicycle are impatient to go on a trip. The bicyclist himself is the best judge of his riding and physical ability. In general, it is best to practice vigorously before taking a trip. Physical condition is the yardstick. During practice, runs should be increased each time until one can easily cycle the distance of the proposed trip. If you want to ride 15 or 20 miles a day or more, strive for that distance. You will tend to work up speed and endurance in practice sessions. If a trip is not planned properly, trouble may ensue. You may not know the road; you may miss picturesque scenery or interesting historical places; or you may find yourself without food or shelter. Steep inclines or mountains may unexpectedly loom up, whereas they seemed perfectly level on the map. Therefore, wise planning will always make a trip easier to undertake.

In order to know where highways and byways are, and their exact elevation, it is necessary to secure two different types of maps: first, a topographical map and, second, a regular road map. The Department of Conservation of the U. S. Geological Survey in Washington, D. C., will send, on request, topographical maps of the localities you plan to visit. These maps cost 10 cents, and their chief value is to enumerate the number of hills you have to climb and the relative height of these hills. The items to be taken along on a trip depend chiefly on the type of the contemplated trip, its duration, and the individual needs of the bicyclist. If camping is intended, then blankets, sleeping bags, tents, and cooking equipment are necessary.

When purchasing a bicycle, be sure that you obtain the right bicycle for you. More bicycles are manufactured in the United States than in any other country in the world. While bicycles are imported from England, Italy, and France, American bicycles are a little cheaper in price. Lightweight wheels are usually selected by bicyclists who want to make trips easier and faster. There is a new type of bicycle called the Compax, which is a folding model used by paratroopers during World War II. Apartment dwellers prefer this model because it can be folded and placed in a closet. Then there is the Tandem which seats two people. Front and rear riders share the task of peddling. The rear handlebars are immovable and merely serve as a grip. The Tandem bicycle is a romantic carry-over from the 1890's when "you looked sweet upon the seat of a bicycle built for two."

For anyone who has never ridden a bicycle the only way to build up confidence is to take the bicycle by the handle bars and start riding. Of course, it is more comforting to have someone with a thorough understanding of the fundamentals of riding demonstrate how this is done, but by and large it is through the process of trial and error that you teach yourself how to ride. George Bernard Shaw, famous playwright, critic, and veteran bicyclist, had this advice to give: "To learn bicycling, try to stand a penny on its edge. Impossible when the penny is stationary, easy when it is rolling. Once convinced of this, rush the machine and jump on."

Bicycle manufacturers like to remind us that the bicycle is probably the oldest article still being manufactured in which the basic principles have changed least. Forerunners of the bicycle go back to about 1819, when the hobbyhorse was a popular fad in France and England. The first bicycles or walking pogo sticks had a saddle, two crude wheels, and a heavy wooden bar. They were difficult to ride because this strange contraption had no pedals. The rider actually had to learn to walk on wheels. London dandies, sitting high in their saddle, rode their hobbyhorses by walking while half-sitting. A strong man could move a little faster than he could walk, but he had to wear stout iron boots. When the bicycle obtained its peddle in 1839, it was able to increase its speed. Kilpatrick MacMillan of Scotland took a look at the hobbyhorse, decided there must be a better way to make the wheels go round, and brought out the first peddle bicycle. It had a wooden frame and the wheels had wood spokes. The driving mechanism consisted of a series of cranks, rods, and hinges which in some remarkable fashion connected with the front. In 1862 Pierre Lallemant, a Frenchman, produced a real iron monster. He called it the velocipede. The bicycle received its present name in 1869 when J. I. Stassen applied for a "bicycle" patent in England. Hollow iron was substituted for wood, light metal replaced heavy iron, and ball bearings were subsequently added.

The bicycle, which is staging a dramatic revival in the United States, has never lost its popularity in Europe. In European countries the cost of gasoline is very high, hence almost every family has a bicycle. For example there are more bicycles in Belfast, Ireland, than there are automobiles. In Copenhagen, Denmark, one out of every three people owns a bicycle.

During the past 10 years manufacturers have done a great deal to streamline the bicycle by giving it sleek lines and less wind resistance. If traffic continues to increase, as is most likely, it is conceivable that doctors in the future will make house calls on bicycles, traversing special paths constructed to control bicycle traffic.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Perforation of Tuberculous Lymph Nodes into the Bronchi in Other than Primary Infections. A. Levi-Valensi. C. Molina and A. Zaffran. Presse méd. 66:523-524 (March 26) 1958 (In French) [Paris].

The intrabronchial perforation of mediastinal lymph nodes is a well-known occurrence in children with primary tuberculous infection, but the fact that similar perforations may occur in adults with other than primary infections has become known more recently, having first come to the authors' attention in 1949. Bronchoscopic examination of 750 tuberculous adults seen in the tuberculosis clinic of the Faculty of Medicine of Algiers in the next 7 years showed that 300 had intrabronchial perforations. A full report on this subject is to be presented to the next National Congress on Tuberculosis; consequently, this paper is limited to an introductory statement of the authors' findings. The patients, 256 of whom were Mohammedans and 44 Europeans, were studied bronchoscopically on request, because of clinical, radiologic, or bacteriological symptoms drawing attention to the bronchi. The preponderance of Mohammedan patients reflects the composition of the authors' service and has no significance in connection with the frequency with which perforation occurs. Intrabronchial perforations, in fact, were found in 46% of the Europeans and in 38% of the Mohammedans, or 40% of the series as a whole. Ordinary pulmonary tuberculosis was present in 258 of the patients, 3 had localized tuberculosis affecting the mediastinal lymph nodes or the pleura, and 29 had hemoptysis without apparent cause. The bronchoscopic appearance varied: some patients presented punched-out perforations with anthracotic secretions, some had small holes, and some had cicatricial fistulas. The lesions were unilateral in five-sixths of the cases, appearing 3 times out of 4 in the right bronchial tree and especially (46.5%) at the point of origin of the upper lobar bronchus. The bronchoscopic findings were confirmed in some cases by autopsy; thus, caseous lymph nodes were found in 18 of 36 subjects, and in 12 of these intrabronchial perforation had occurred. The perforations, which were moderate in size and usually showed anthracotic pigmentation, were associated with various lesions characteristic of pulmonary tuberculosis. Histological study enabled the authors to trace the passage connecting the depression in the mucosa with the fibrocaseous lymph node. Islets of anthracotic pigment and an absence of glands and muscle fibers are the two main characteristics by which the passage can be identified.

The Occurrence of Arrhythmias in Acute Myocardial Infarctions. C. C. Johnson and P. F. Miner. Dis. Chest 33:414-422 (April) 1958 [Chicago].

The authors report on 142 men and 45 women, between the ages of 31 and 90 years, with acute myocardial infarction, who were treated at 2 community general hospitals in the course of 5 years. These 187 patients were a group representative of all economic and social spheres. Arrhythmias, with the exclusion of extrasystole and bundle-branch block, occurred in 31 (16.5%) of the 187 patients. The most common type of arrhythmias was auricular fibrillation which occurred in 16 (8.7%) of the 187 patients; it occurred in 8 (9.1%) of the 89 patients with anterior infarction and in 8 (8.2%) of the 98 with posterior infarction. Atrioventricular block was noted in 11 patients (5.9%), 10 of whom had posterior infarction. Ventricular tachycardia occurred in only 1 patient, and this patient had posterior infarction. Auricular flutter was observed in 1 patient, and nodal tachycardia in 2. Complicating factors were hypertension occurring in 56 patients, shock in 27, and heart failure in 29. Of the 187 patients, 44 died, representing an overall mortality rate of 23.5%. Nine (29.2%) of the 31 patients with arrhythmias died, and 35 (22.4%) of the 156 patients without arrhythmias died. The mortality rate among patients with heart failure and myocardial infarction was 49%, that among patients with shock and myocardial infarction was 52%, and that among patients with auricular fibrillation was 31%. Two of the 7 patients with complete heart block died. The mortality rate was higher (55%) among patients with arrhythmias occurring with anterior infarction than was this rate (45%) among patients with arrhythmias occurring with posterior lesions. This may have been due to the fact that heart failure occurred twice

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The place of publication of the periodicals appears in brackets preceding each abstract.

Periodicals on file in the Library of the American Medical Association may be borrowed by members of the Association or its student organization and by individuals in continental United States or Canada who subscribe to its scientific periodicals Requests for periodicals should be addressed "Library, American Medical Association" Periodical files cover 1949 to date only, and no photoduplication services are available No charge is made to members, but the fee for others is 15 cents in stamps for each item Only three periodicals may be borrowed at one time, and they must not be kept longer than five days Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order Reprints as a rule are the property of authors and can be obtained for permanent possession only from them as often in anterior as in posterior infarction. There was a mortality rate of 20.3% among men and of 33.3% among women. The exact mechanism of arrhythmias remains unknown. Anoxia of the myocardium would seem to be the important factor involved in auricular fibrillation.

The Sleeping Pulse Rate in Thyrotoxicosis. J. Crooks and I. P. C. Murray. Scottish M. J. 3:120-122 (March) 1958 [Glasgow].

The development of many accurate tests for the diagnosis of hyperthyroidism has resulted in a neglect of simple clinical methods. One such method is the recording of the sleeping pulse rate. Ranges of normality had never been established for this method, and so the authors investigated those and evaluated the sleeping pulse rate as an aid to the diagnosis of thyrotoxicosis. The study comprised 246 subjects. In 166 patients (69 nontoxic, 97 toxic), the diagnosis was definite on clinical grounds and was confirmed by radioiodine studies. In 80 patients (39 nontoxic, 41 toxic), the diagnosis was classified as doubtful, the criterion for inclusion in this group being that diagnostic difficulty had been found. The record of the sleeping pulse rates in 108 nontoxic and 138 toxic subjects showed that 53.7% of the toxic but only 2.8% of the nontoxic subjects had sleeping pulse rates greater than 80 beats per minute. When, therefore, 80 beats per minute was taken as the upper limit of the normal range of sleeping pulse rates, the diagnostic value of the procedure could be seen in clinically obvious cases and in cases where there was initial doubt as to the diagnosis. Of the unequivocally toxic subjects, 64% had elevated sleeping pulse rates, but this was observed in only 29% of the doubtful group. Thus, rates of more than 80 per minute make the diagnosis of thyrotoxicosis highly probable. Slower rates have no diagnostic significance. Seventy-one per cent of the patients with hyperthyroidism who had given initial diagnostic difficulty had sleeping pulse rates less than 81 beats per minute. There was no statistically significant correlation between the sleeping pulse rate and the degree of clinical severity of the disease.

The Syndrome of Hypoparathyroidism. Addison's Disease and Moniliasis. B. S. Hetzel and H. N. Robson. Australasian Ann. Med. 7:27-33 (Feb.) 1958 [Sydney, Australia].

Idiopathic hypoparathyroidism is a rare condition, less than 80 cases being recorded in the literature. It is, therefore, a matter of some surprise and interest to find that in at least 7 patients, all juveniles, this condition has been accompanied by Addison's disease, itself a rare disorder in the first decade of life. Chronic moniliasis has also been a feature of several of these cases. An 8th case of the rare combination of idiopathic hypoparathyroidism and Addison's disease is reported. A girl, aged 16 years, had had epileptic fits since the age of 10. Investigations showed cerebral calcification, with low serum calcium, raised inorganic phosphorus, and normal urea nitrogen values. The patient also showed typical clinical and biochemical features of Addison's disease. Treatment with cortisone and large doses of dihydrotachysterol (A. T. 10) led to improvement in the patient's clinical state and also in her IQ, electroencephalogram, and electrocardiogram. The initial administration of cortisone led to a fall in the serum calcium level, and, subsequently, the control of Addison's disease necessitated administration of larger than usual doses of dihydrotachysterol. The authors feel that the clinical course of this and other previously reported cases provides some evidence of an antagonism between the parathyroid and the adrenal glands.

An Aerosol Method of Producing Bronchial Secretions in Human Subjects: A Clinical Technic for the Detection of Lung Cancer. H. A. Bickerman, E. E. Sproul and A. L. Barach. Dis. Chest. 33:347-362 (April) 1958 [Chicago].

Inhalations for periods of 10 to 20 minutes of an aerosol produced by the continuous nebulization of a solution containing 10 or 15% sodium chloride and 20% propylene glycol and warmed to 105 to 130 C were used in 336 patients to induce sputum production. The patients were divided in 3 groups. The first group consisted of 203 patients with a wide variety of diseases but with no evidence of pulmonary disease by clinical or roentgenologic study. The second group consisted of 110 patients with chronic nontuberculous pulmonary disease in whom the diagnosis of bronchial asthma, pulmonary emphysema, and chronic bronchitis predominated. The third group consisted of 23 patients with known or suspected malignancy involving the lung or other organs. All the material expectorated during, and for 10 minutes after, the aerosol inhalation was collected and measured. Of 203 patients in the first group, 23 had neurological disorders with marked impairment of the cough mechanism and were, therefore, excluded. After the inhalation of hypertonic sodium chloride solution by the remaining 313 patients, specimens of sputums suitable for cytological examination were recovered from 277 (88.5%). Of special interest as a possible screening technique for the cytological diagnosis of lung cancer was the production of sputum in 86% of the 180 patients in the first group who had no evidence of pulmonary disease and no cough or spontaneous sputum. Only 3 of these noted a slight irritation on inhaling the warm 10% sodium chloride solution.

Cytological studies of the sputum recovered from 74 patients (27 of the first group, 28 of the second, and 19 of the third) after inhalation of the sodium chloride solution showed that 79% of the specimens were satisfactory for diagnosis. In 5 of the 8 patients with documented primary or metastatic carcinoma of the lung, sputum preparations were positive for malignant cells. There were no false-negative reports. Since all the examinations were performed on single specimens, it is evident that cytological study of repeated specimens obtained in a similar manner might increase the possibilities of accurate diagnosis. This method of inducing sputum may be expected to show tumor cells from symptom-free persons before spontaneous sputum arises, since the specimens obtained by inhalation of the hypertonic sodium chloride solution are entirely adequate for study.

Parietal Pleural Needle Biopsy. J. D. Welsh. A. M. A. Arch. Int. Med. 101:718-721 (April) 1958 [Chicago].

Needle biopsy of the parietal pleura was performed on 4 men and 13 women, between the ages of 17 and 78 years, who were selected because they either presented pleural effusion as a diagnostic problem or were suspected of having a neoplasm or tuberculosis. After the biopsy specimen was obtained, a thoracentesis was performed through the already anesthetized site. When possible, information was obtained about protein, cell count, microscopic examination of cell block for malignant cells, cytology, and culture of pleural fluid. Fourteen of the 17 patients were proved to have neoplastic involvement of the pleura. Positive biopsy specimens were obtained from 10 of the 14 patients. In 3 of the 10 patients the cell block and cytological examinations were negative, while the findings of the biopsy were diagnostic. Two patients did not have pleural fluid, and the diagnosis of neoplasm was made only on the basis of the biopsy. In an additional patient the biopsy specimen was positive for neoplasm, but no studies were done on the pleural fluid. In 3 of the 4 remaining patients with diagnostic biopsy specimens, both cell block and cytological examinations also gave positive results. In the last patient with a positive biopsy specimen, the cell block examination gave a positive result, while the cytological examination was negative. Negative biopsy specimens were obtained from 4 of the 14 patients with proved neoplastic involvement of the pleura. Three of these 4 patients had positive results from either cell block or cytological examination, and all studies gave negative results in the 4th patient. From the remaining 3 of the 17 patients noncontributory biopsy specimens were obtained; in these patients a diagnosis has not been established after 1 to 1½ years.

Needle biopsy of the parietal pleura is an easy method which can even be carried out in outpatients. Complications are not any greater than with routine thoracentesis if suitable precautions are used. The method is useful but not foolproof, and a negative biopsy specimen does not rule out tuberculosis or neoplasm. In a few cases the final answer will come only from thoracotomy, long follow-up, or autopsy.

Penicillin Therapy in Treatment of Ulcer Disease. O. L. Gordon, G. F. Markova, V. A. Oleneva and P. D. Tarnopolskaya. Klin. Med. 36:22-26 (Feb.) 1958 (In Russian) [Moscow].

The authors report on penicillin therapy of complicated, intractable gastric and duodenal ulceration. There were 67 men and 33 women, with involvement of the stomach in 30 patients and of the duodenum in 61 and with gastroduodenal ulceration in 9. Forty patients presented various complications of gastric function and an active perigastritis. Sixty-one patients had complications of other organs of nutrition, most frequently of the liver and biliary tracts. Eighty-two patients had had symptoms for more than 6 years, 45 of these for more than 10 years. Eighty-six patients had received hospital treatment in the past. The authors recommend intramuscular injection of 200,000 to 300,000 units of penicillin 2 to 3 times daily, the total being 6 to 10 million units for a course of treatment. Roentgenologic studies demonstrated a niche before the treatment in 36 patients with gastric ulcer and in 47 patients with duodenal ulcer. Under the influence of penicillin therapy the niche disappeared in 48 patients, was hardly recognizable in 17, diminished significantly in 9, and was not changed in 9. The authors consider penicillin therapy as a valuable ancillary method of treating ulcers in complicated cases. Penicillin therapy is indicated in cases with inflammatory infiltration of the edges of the ulcer, in cases with inflammatory lesions of the biliary tracts, and in cases with active plastic perigastritis. In addition to the curative effect, administration of penicillin aids in differentiation between inflammatory and malignant infiltration of the borders of the ulcer.

The Secretor Status in Duodenal Ulcer. J. Wallace, D. A. P. Brown, I. A. Cook and A. G. Melrose. Scottish M. J. 3:105-109 (March) 1958 [Glasgow].

A significantly increased incidence of blood group O among patients with peptic ulceration has been reported, and subsequently it was shown that the excess of group O was confined to patients with duodenal ulcer, particularly to those requiring operation. A continued study of the group O excess in patients with duodenal ulcer seemed indicated, particularly with reference to the severity of duodenal ulceration and to the suggestion that the mucopolysaccharide nature of the ABH substances secreted might have a protective action on the mucosa of the gastrointestinal tract. The concentration of blood group substances is higher in saliva and in gastric juice than in most other body fluids. The presence of group A substance in body fluid is shown by the ability to inhibit or neutralize the specific action of anti-A on group A red blood cells. Group B substance is similarly demonstrated by its specific action on anti-B serum. Secretors of group O have in their saliva H substance which is not group-specific, being found also in secretors of groups A, B, and AB. The presence of H substance is detected by the inhibition of anti-H which occurs naturally in eel serum and in extracts of the seeds of certain leguminous plants. The authors studied the secretor status of 214 patients of blood groups A, B, and AB and of 201 patients of group O who had peptic ulcer. Appropriate control series were studied for comparison. In groups A, B, and AB secretor activity was determined by the examination of saliva for group-specific substances. The probable secretor activity in group O cases was based on the reaction between red blood cells and anti-Le^a serum. There was a significant excess of nonsecretor individuals among patients with duodenal ulcer. It was mainly the patients in whom a diagnosis was made at operation, that is, the more severe cases, who contributed to the excess of nonsecretors. It is suggested that mucopolysaccharides which contain the blood group substances have a protective action on the mucosa of the gastrointestinal tract. Secretor status in peptic ulcer may be of prognostic value, and the absence of blood group substances may be an additional indication for surgical treatment.

Mortality of Patients with Diabetic Acidosis in a Large City Hospital. T. G. Skillman, R. Wilson and H. C. Knowles Jr. Diabetes 7:109-113 (March-April) 1958 [New York].

The authors report observations on 312 patients, admitted to the Cincinnati General Hospital between 1947 and 1956, in whom the serum carbon dioxide content was 14 mM. per liter or less due to ketosis, and who lived for at least 3 hours after institution of insulin therapy. A patient was considered to have survived from diabetic acidosis if he was alive 30 days after admission. Of the 312 patients, 140 were admitted to the hospital and treated in the course of the first 5 years of observation period, and 172 during the second 5-year period. Forty-four of the 140 patients died, representing a mortality rate of 31.4%, as compared with 25 of the 172 patients, representing a mortality rate of 14.5%. Nonacidotic complications, potentially fatal in themselves, such as infection, vascular disorders, and miscellaneous conditions, occurred in 23 of the 140 patients and in only 9 of the 172 patients. The mean amount of insulin administered in the second 5-year period was 64 units greater than in the first period. Bicarbonate averaging 150 mEq. per patient was given to 116 patients in the second period, in contrast to 32 patients in the first period. The potassium administered parenterally in the first period was not only given infrequently but was also less in amount, averaging 35 mEq. per patient in the first period as compared with 49 mEq. per patient in the second period. Arterenol for sustained hypotension was not available in the first period but was given to 17 patients in the second period. The authors believe that a lower incidence of nonacidotic complications was in large part responsible for the decline in mortality. Although it could not be shown that altered therapy caused increased survival in those patients without severe complications, the use of arterenol and the parenteral administration of potassium appeared to be lifesaving in certain cases.

Effect of Smoking on the Production and Maintenance of Gastric and Duodenal Ulcers. R. Doll, F. A. Jones and F. Pygott. Lancet 1:657-662 (March 29) 1958 [London].

A comparison was made of the smoking habits of patients with and without peptic ulcer, and the effect of advising patients to stop smoking was tested by a controlled clinical trial. Each ulcer patient was matched by 2 controls chosen to resemble the ulcer patient in sex, age, place of residence, and (for male patients) socioeconomic class. There were 232 patients with gastric ulcer and 448 control patients; for 278 patients with duodenal ulcer there were 535 control patients. The percentage of nonsmokers was less among the ulcer patients than among the controls both for gastric ulcers and for duodenal ulcers and in both sexes. In contrast, no appreciable differences were found between the proportions of heavy smokers. More of the men with gastric ulcers than of their controls had begun to smoke before the age of 15, and less had begun to smoke at the age of 30 or more. No important differences in the age at starting to smoke were found in the other groups. With both types of ulcer the proportion of smokers who smoked only cigarettes was higher in the ulcer groups than in the controls.

These results may be interpreted in several ways; therefore, further evidence was sought in a clinical trial. Inpatients with gastric ulcers who, on admission to hospital, were regular smokers were divided at random into 2 groups. In 1 group the patients were advised to stop smoking; in the other they were given no such advice. All the patients were treated in bed for 4 weeks, and all other treatments were prescribed equally in both groups. Among 40 patients advised to stop smoking, the ulcer healed by two-thirds or more in 30, and the average reduction in the size of the ulcer niche was 78.1%. Among 40 patients not advised to stop smoking, the ulcer healed by two-thirds or more in 23, and the average reduction in the size of the ulcer was 56.6%. The ulcer healed by two-thirds or more in a higher proportion of those who followed the advice (19 of 22) than it did in those who reduced their smoking but did not stop completely (11 of 18); the average reduction in the size of the ulcer was also greater in the former group. The average gain in weight and the severity of symptoms were not significantly different in the group of patients advised to stop smoking and in the controls. The results accord with 3 recent studies of the mortality and morbidity of peptic ulcer in relation to smoking habits, and it is concluded that, in some patients, smoking interferes with the healing of a peptic ulcer and helps to maintain its chronicity.

A Haemoglobinopathy Involving Haemoglobin H and a New (Q) Haemoglobin. F. Vella, R. H. C. Wells, J. A. M. Ager and H. Lehmann. Brit. M. J. 1:752-755 (March 29) 1958 [London].

Electrophoretic studies on hemoglobin from adults had demonstrated that hemolysates obtained from erythrocytes of patients with sickle-cell anemia exhibited properties that differed greatly from those of hemolysates from erythrocytes of normal adults. This discovery of the usefulness of electrophoresis in the study of hemoglobin has led to recognition of other variants of adult human hemoglobin. The authors describe the properties of a new hemoglobin which was detected in association with hemoglobin H and describe the clinical and other findings in the patient presenting this new hemoglobinopathy. The patient was a 24-year-old Chinese who was first admitted to the Singapore General Hospital in August, 1953, with a history of shortness of breath, palpitation, giddiness, blurring of vision, and precordial pain on exertion, associated with anorexia and generalized edema. He was found to have a gross hypochromic anemia. The further course of the anemia indicated that it was chronic and did not respond to iron therapy. Roentgenograms of the chest revealed no abnormalities, but those of the skull and hands revealed small translucent areas.

A film of the peripheral blood stained with Leishman's stain showed hypochromia, anisocytosis, poikilocytosis, polychromasia, and many target cells. Supravital staining with brilliant cresyl blue showed inclusion bodies in about 95% of the erythrocytes, as is seen in blood which contains hemoglobin H. Resistance to lysis was increased. There was no sickling with 2% sodium metabisulfite, and there were no siderocytes. Paper electrophoresis at pH 8.6 showed 2 components in fresh blood samples. The smaller, comprising 20% of the total, had the mobility of hemoglobin H or hemoglobin I, and the remainder moved between hemoglobins A and S. At pH 6.5 the smaller fraction moved toward the anode, which is the unique property of hemoglobin H. Further studies on the nonhemoglobin H component revealed certain similarities to hemoglobin S and hemoglobin G, but it differed from all known hemoglobins in its electrophoretic behavior on paper electrophoresis at pH 8.6, although the difference from hemoglobin G was small. It also differed from all other known hemoglobins in its chromatographic behavior. The following hemoglobins are now known: A, C, D, E, F, G, H, I, J, K, L, M, and S. The letter N is being reserved for a new hemoglobin from Liberia. Two other abnormal hemoglobins have been described, which are provisionally known as Buginese X and the Galveston type respectively. The new hemoglobin has been found to differ from them all on paper electrophoresis at pH 8.6 and on resin chromatography. Leaving the letters N, O, and P for the naming of the hemoglobins from Liberia, Indonesia, and Texas, the authors apply to the new pigment the term "hemoglobin Q" and to the hemoglobinopathy observed in the aforementioned patient the term "hemoglobin Q-H disease." The mother, who is the only member of the patient's family available for study, has been found to be an asymptomatic carrier of hemoglobin Q.

"These Dying Diseases": Venereology in Decline? A. King. Lancet 1:651-657 (March 29) 1958 [London].

In Britain and other Western countries the incidence of the venereal diseases during the past 25 years has followed an expected trend—a steady decline during the 1930's, during times of peace and in association with more diligent methods of venereal disease control, followed by a great rise during the years of war; this rise reached a peak in 1946, a year after World War II ended, and was followed by a steep decline during years of peace and plenty in which new and effective remedies became increasingly available. Commenting on graphs showing (1) the number of cases of syphilis of less than a year's duration, (2) the number of cases of more than a year's duration, and (3) the mortality from late syphilis, the author suggests that the figures indicate trends rather than true incidence. He feels that infectious syphilis often remains undiagnosed. Therefore, a rise in the incidence of late syphilis might be expected as a result of the high prevalence of early syphilis during and after the last war. The reported figures do not bear this out. Whatever the truth about the prevalence of late syphilis, there can be no doubt about the decline in mortality from the late manifestations. The reported incidence of congenital syphilis has shown a steady decline.

Discussing gonorrhea, the author cites figures from British clinics and comments from the United States. A new increase was noted in some urban areas in Britain during 1956, and it continued in 1957. The author feels that pronouncement about this increase must be largely speculative, but he suggests that emergence of penicillin-resistant strains of gonococci and immigration from other parts of the Commonwealth might be responsible. The importance of prostitutes in spreading gonorrheal infection should not be underestimated. Chancroid has declined from an incidence which was never high. Nonspecific genital infection is now recognized as a major and growing problem. Lymphogranuloma venereum is seldom diagnosed, but there is reason to suppose that it is not rare. Cases of granuloma inguinale are beginning to appear in small numbers. It should be noted that the decline in incidence of some venereal diseases has not been accompanied by a similar fall in the total number of new patients attending the treatment centers.

The venereal diseases, despite persistent rumors to the contrary, are not dead or even dying. Even in present favorable circumstances they are a considerable problem. Modern developments have in some respects complicated their management. The reduction in venereal diseases since World War II probably owes more to favorable social conditions than to new remedies. The postwar decline in incidence and the introduction of new remedies have inspired a false confidence and a move to dismantle some of the organizations which have helped to control these diseases. Although the venereal diseases are certainly not dying, there is danger of the decline of venereology. The combination of thriving diseases and the disappearance of those specialists whose study they are has obvious dangers for the public health.

Hypercalcemia in Sarcoidosis: Case Treated with Diet Low in Calcium. P. J. Dragsted and N. Hjorth. Ugeskr. læger 120:245-248 (Feb. 20) 1958 (In Danish) [Copenhagen].

Sarcoidosis with spontaneous hypercalcemia has often been mistaken for hyperparathyroidism. In hypercalcemia it is advisable to include sarcoidosis in the diagnostic considerations. Hypercalcemia in Boeck's sarcoid can be prevented by low-calcium diet. Beginning hypercalcemia usually manifests itself by thirst and polyuria. A developed hypercalcemia should be treated with a diet low in calcium, supplemented possibly with steroid preparations. In a case of sarcoidosis localized to the eyes and lungs and complicated with spontaneous hypercalcemia and metastatic changes under the cornea epithelium, treatment with calciferol was followed by beginning uremia and development of calcifications around the joints. Low-calcium diet, continued for 5 years, has resulted in disappearance of the metastatic calcifications, normalization of the serum calcium level, and improvement in the renal function, and the cornea calcifications have not recurred.

The Latex Agglutination and Inhibition Reactions: Clinical Experience in the Diagnosis of Rheumatoid Arthritis. A. P. Hall, A. D. Mednis and T. B. Bayles. New England J. Med. 258:731-735 (April 10) 1958 [Boston].

The serum from patients with rheumatoid arthritis has been found to agglutinate certain strains of streptococci, and also sheep cells sensitized with rabbit anti-sheep-cell serum. This serum contains a factor (or factors) that is either absent or present in only minimal amounts in the serum of normal persons. Rose and others described in 1948 the first diagnostic test for rheumatoid arthritis with sensitized sheep cells. Many variations and modifications of the Rose test have been described. Heller and co-workers substituted human gamma globulin for rabbit serum in sensitizing sheep cells. Singer and Plotz substituted latex particles for sheep cells. Ziff and associates, in order to increase the sensitivity of the sheep-cell test, employed an inhibition procedure; in this test the euglobulin fraction of the unknown serum was tested for its ability to inhibit the agglutination of sheep cells by a known positive rheumatoid serum.

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The 3-step latex procedure was used to test 1 or more samples of serum from 582 patients. These patients belonged to 3 groups. There were 177 patients considered to have definite rheumatoid arthritis (group A), 164 patients classified as having musculoskeletal disease presenting diagnostic problems (group B), and 135 patients, of whom 44 were normal controls, not considered to have rheumatoid arthritis (group C). The 3-step latex test proved to be a valuable and highly sensitive procedure for use in the diagnosis of rheumatoid arthritis. It gave positive results in 99.4% of the patients with known rheumatoid arthritis (group A), in 57.9% of the patients with diagnostic musculoskeletal problems (group B), and in 5.2% of the patients who did not have rheumatoid arthritis (group C). The test, although requiring meticulous attention to detail, proved practical for routine use.

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The positive outcome of the latex fixation tests in the patients with rubella arthritis was unexpected, and several possible explanations are considered. The tests may represent a laboratory error, since the positive results were almost entirely in the inhibition step, which is the most difficult step to read. However, it seems unlikely that the same error would not be present in the controls to the same degree. The positive results may be explained on the basis of inheritance of the "rheumatoid factor," although family histories do not show this consistently. The latex test may not be specific for a "rheumatoid factor," and in the cases referred to above may have represented a nonspecific alteration of serum protein in response to an infection. The test may be specific for a "rheumatoid factor." If so, the factor was either present in the blood of the Framingham patients before the onset of rubella (by way of inheritance or by a previous unrecognized attack of rheumatoid arthritis) or developed as a result of a first attack of rheumatoid arthritis after rubella or another illness clinically indistinguishable from it.

Timely Versus Delayed Use of the Artificial Kidney. P. F. Salisbury. A. M. A. Arch. Int. Med. 101:690-701 (April) 1958 [Chicago].

Of 51 patients, between the ages of 16 and 79 years, with acute anuria treated by the author with or without hemodialysis, 34 recovered and 17 died, although potentially reversible acute tubular necrosis was found in the latter at autopsy. The treatment of the patients who recovered and that of those who did not recover from reversible renal failure was compared, and an attempt was made to identify errors made in the management of those who died and to formulate specific clinical situations which should call for hemodialysis without delay. Of the 34 patients with acute anuria who survived, 19 recovered without the use of dialysis. The duration of anuria-oliguria in these patients was from 3 to 11 days. The maximum serum creatinine level was 18 mg. per 100 cc., the maximum blood urea nitrogen content was 195 mg. per 100 cc. The standard treatment consisted of limitation of fluids to the visible output and an additional 500 to 700 cc. for the loss by insensible perspiration minus water of oxidation. The remaining 15 of the 34 patients were treated with hemodialysis. The duration of anuria-oliguria was from 9 to 39 days. The maximum nonprotein nitrogen content was 280 mg. per 100 cc., and the highest blood urea nitrogen level was 219 mg. per 100 cc. The highest serum potassium level was 10.2 mEq. per liter. In 12 of these 15 patients the artificial kidney procedure was considered lifesaving.

Of the 17 patients with acute reversible renal disease and without associated primary pathological lesions who died, 7 were treated with hemodialysis, but hemodialysis was not used in 10. One error which was made in the management of all 17 patients who did not recover consisted in delay in the use of the artificial kidney. Observations made on these 17 patients showed that the terminal stage of acute uremia, characterized by coma, convulsions, or severe cardiac failure, is often not reversible with or without dialysis, that the condition of patients in the preterminal stage frequently deteriorates within a matter of hours into the terminal stage, and that irreversible (or slowly reversible) injury to the nervous or circulatory systems can occur early, i.e., before the 10th day, in the course of acute anuria. The following indications are now given for dialysis: 1. The existence of an electrolyte abnormality (serum potassium level is above 7 mEq. per liter; blood carbon dioxide contents are below 12 mEq. per liter). 2. Clinical signs and symptoms of uremia present on the 5th day of anuria-oliguria, such as drowsiness, confusion, irritability, hostility, restlessness, ankle clonus, hyperactive reflexes, slight papilledema, and edema of the retina (nervous signs or symptoms), and tachycardia, slight pulmonary congestion, and increased second pulmonic sound (cardiovascular signs); vomiting, retching, ileus, and persistent wrinkling of the scrotum and areola mammae are other signs and symptoms which should be indication for dialysis. 3. In the absence of such clinical signs and symptoms dialysis is indicated on the 6th day of anuria-oliguria. 4. Dialysis should be repeated whenever indicated clinically, or by serum electrolytes or by a blood urea nitrogen level above 150

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retinal artery [illegible] of occlusion. In none of the 4 patients presented was the patient's condition made worse by the operation. The technical difficulties in attempting to clean a thrombus from the intracranial portion of the internal carotid artery can be formidable because of the tortuosity of the vessel in this area and the lack of exposure. In only 2 of the 4 patients was it possible to reestablish flow through the vessel. Significant neurological improvement was

treatment of the patients who recovered and that of those who did not recover from reversible renal failure was compared, and an attempt was made to identify errors made in the management of those who died and to formulate specific clinical situations which should call for hemodialysis without delay. Of the 34 patients with acute anuria who survived, 19 recovered without the use of dialysis. The duration of anuria-oliguria in these patients was from 3 to 11 days. The maximum serum creatinine level was 18 mg. per 100 cc., the maximum blood urea nitrogen content was 195 mg. per 100 cc. The standard treatment consisted of limitation of fluids to the visible output and an additional 500 to 700 cc. for the loss by insensible perspiration minus water of oxidation. The remaining 15 of the 34 patients were treated with hemodialysis. The duration of anuria-oliguria was from 9 to 39 days. The maximum nonprotein nitrogen content was 280 mg. per 100 cc., and the highest blood urea nitrogen level was 219 mg. per 100 cc. The highest serum potassium level was 10.2 mEq. per liter. In 12 of these 15 patients the artificial kidney procedure was considered lifesaving.

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analgesic blocking treatment [illegible] ganglion also underwent resection of the cervical sympathetic nerve. Of these patients, 18 had thrombosis, 1 had embolism, and 1 had cerebral hemorrhage. Simple stellectomy with resection of a part of the cervical sympathetic chain was performed on 7 patients. This procedure was combined with pericarotid and perivertebral sympathectomy in 13 patients. Operation was homolateral on the side of the cerebral lesion in 5 patients and bilateral in 15.

mg. per 100 cc. If these criteria for hemodialysis had been followed, most of the 17 patients now dead would probably have survived. Of the 34 patients who survived, only an additional 6 would have been treated with hemodialysis when this was not necessary for their survival.

Psychosomatic Study of 18 Patients with Hemorrhagic Rectocolitis. M. de Muzan, S. Bonfils and A. Lambling. Semaine hôp. Paris 34:922-928 (March 28) 1958 (In French) [Paris].

The authors report on a psychosomatic study of 18 patients, 13 women and 5 men, ranging in age from 16 to 48 years, with hemorrhagic rectocolitis. The purpose was to explore the environment, personality, and childhood of each patient in order to arrive at a better understanding of the basic mechanism of the disease and thus to provide for more effective treatment. The personality of these patients was characterized by an ambivalent attitude toward others, psychoneurotic manifestations with predominantly depressive features, sexual disturbances which were especially marked in women, and frequently a maladjustment to the social and family environment. An emotional strain often precedes either the onset or the recurrence of the disease, which is elicited by grief, by actual or anticipated abandonment, or by the necessity of assuming a new responsibility. Severe emotional disturbances marked the childhood of most of these patients, and these early experiences provided the elements which later played a dominant part in their relations with other persons and in the circumstances precipitating the disease. The psychosomatic aspects of patients with rectocolitis, which have already been described by other workers, are closely connected with depressive conditions. The similarity between the psychological structure of patients with depressive conditions and that of patients with hemorrhagic rectocolitis warrants the conclusion that the degree of regression in rectocolitis is the same as that found in depressive conditions, i. e., the oral-sadistic stage. This notion provides for a better understanding of the patient's attitude, the part played by the precipitating circumstances, and the significance of certain aspects of the course of the disease.

Benign Mucous-Membrane Pemphigus. P. L. Mc- [illegible] cemia usually [illegible]

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junctiva and the oral mucosa, are characteristically involved, and the lesions tend to produce scarring, although this is not a common complication of oral vesiculations. Benign mucous-membrane pemphigus is a rare entity but not as uncommon as often supposed. The authors report and evaluate the features of 15 cases of benign mucous-membrane pemphigus seen in private practice, in consultation, and in the oral medicine clinic of Tufts University. The age at onset ranged from 23 to 75 years. The diagnosis was made on the basis of the history and clinical appearance of the lesions.

The microscopic picture is important in excluding pemphigus vulgaris and other lesions. The similarity of so-called chronic desquamative gingivitis to the gingival lesions of benign mucous-membrane pemphigus suggests the possibility that some cases initially diagnosed as desquamative gingivitis are, in fact, the early gingival manifestations of benign mucous-membrane pemphigus. These cases should be carefully followed. The absence of acantholysis in this condition indicates that the term "pemphigus" should be dropped and the condition termed "benign mucous-membrane pemphigoid." Further investigations of the etiology are indicated. Steroid therapy has proved reasonably effective in controlling the lesions of benign mucous-membrane pemphigus.

SURGERY

Arteriovenous Angiomas of the Brain in Children. J.-E. Paillas, J. Bonnal, M. Bérard-Badier and G. Serratrice. Presse méd. 66:525-528 (March 26) 1958 (In French) [Paris].

Arteriovenous angiomas of the brain are congenital malformations, but they are seldom diagnosed or treated in children. The authors, therefore, report on 11 patients, aged 4 to 15 years, operated on for removal of a cerebral angioma. These angiomas usually manifest themselves in children, as well as in adults, by either meningeal hemorrhage, cerebral hemorrhage, or epileptic crises. Meningeal hemorrhage was the revelatory symptom in 1 of the patients; an intracerebral hematoma, in 6; and focal epileptic crises, in 4. A diagnosis of angioma can usually be made on the basis of cerebral angiography, although small malformations that have become thrombosed or [illegible] may not be [illegible] diagnostic [illegible]

lems (group B), and 135 patients, of whom [illegible] controls [illegible] may cause only [illegible] tients, 3 of whom were operated on while in coma, speak for themselves: 9 patients recovered, 7 without any significant sequelae, and only 2 died, 1 because the extent of the angioma seemed to make it inoperable and the other because the operation was performed too late.

Internal Carotid Artery Thrombosis. B. Roberts. G. W. Peskin and F. A. Wood. A. M. A. Arch. Surg. 76:483-491 (April) 1958 [Chicago].

It is now appreciated that a considerable number of cerebral vascular accidents are the result of thrombotic occlusion of the carotid artery. In view of the potentialities of vascular surgery today, it is clear that physicians must become aware of the possibility of carotid artery thrombosis and stenosis in the differential diagnosis of patients with a "stroke." Only in this way can the correct diagnosis be established early enough to grant these patients the optimal chance for reestablishment of the circulation and for recovery. Carotid artery thrombosis can be readily overlooked unless the examining physician has a "high index of suspicion." Within the past 6 months the authors observed 5 patients with this difficulty at the Hospital of the University of Pennsylvania. Four of these patients were operated on and constitute the basis of this report. The factors responsible for this condition include thromboangiitis obliterans, trauma, and thrombosis of a cerebral aneurysm, but in the majority of patients arteriosclerosis appears to be the responsible antecedent. The clinical picture of carotid artery thrombosis may follow one of several patterns. Many of the patients give a history of previous transient episodes of paresthesia, aphasia, and hemiparesis, often of gradual onset and rapid disappearance. Headaches, usually on the involved side, are common and generally precede the hemiparesis by a considerable period of time. Convulsions, both localized and generalized, have been reported, and a significant number of cases have been found among patients originally suspected of having a brain tumor.

Diagnostic measures include palpation of the pulse, observation of arterial pressure in the retinal vessels, and carotid arteriography. Arteriography, in which a radiopaque dye is injected percutaneously into the common carotid artery, should be carried out if the findings on palpation or the retinal artery pressure determination are suggestive of occlusion. In none of the 4 patients presented was the patient's condition made worse by the operation. The technical difficulties in attempting to clean a thrombus from the intracranial portion of the internal carotid artery can be formidable because of the tortuosity of the vessel in this area and the lack of exposure. In only 2 of the 4 patients was it possible to reestablish flow through the vessel. Significant neurological improvement was obtained in only 1 of the patients, on whom the operation was performed within 36 hours after occlusion. At the present time the authors are attacking the problem by 2 approaches. Several spring-like reaming instruments have been tested in the internal carotid arteries of cadavers but have not proved satisfactory. Plastic tubing in short lengths has been used as an endarterectomy instrument, and attempts to pass the tube to the level of the carotid siphon succeeded in cadavers but not in patients with thrombosis. The ideal instrument should be flexible enough to traverse the course of the vessel and strong enough to strip the clot and any plaques, and have a central lumen to which suction could be applied. The second approach has been concerned with the finding of a suitable enzymatic agent which will dissolve the thrombus if endarterectomy is not feasible.

Results of Operations on the Cervical Sympathetic Nerve (Analgesic Blocking and Resection) in 95 Patients with Focal Vascular Cerebral Disease. T. Poletti. Minerva med. 49:454-468 (Feb. 10) 1958 (In Italian) [Turin, Italy].

Ninety-five patients with focal vascular cerebral disease, who were over 30 years of age, have received treatment by analgesic blocking of the stellate ganglion. Complete regression of the clinical manifestation of the disease, without or with insignificant sequelae, was obtained in 8 patients (10.7%). Partial results, consisting of partial regression of the clinical symptoms or of full regression of only 1 symptom (aphasia, motor deficit, or psychic disorder), were observed in 43 patients (57.2%). Twenty-four patients (32%) derived no benefit from the therapy. Eleven of these 24 patients died during the period of observation. Best results were obtained in patients with thrombosis. The group included 8 patients in whom complete results and 36 patients in whom partial results were obtained. Patients with embolism or hemorrhage derived only slight benefit from the therapy. The efficacy of treatment in patients with thrombosis and embolism was greater if it was instituted within 72 hours after the episode had occurred. The sooner the injection therapy was begun, the greater were the therapeutic effects. Improvement of symptoms in most instances developed after 4 or 5 injections.

Twenty patients in this series who received analgesic blocking treatment of the stellate ganglion also underwent resection of the cervical sympathetic nerve. Of these patients, 18 had thrombosis, 1 had embolism, and 1 had cerebral hemorrhage. Simple stellectomy with resection of a part of the cervical sympathetic chain was performed on 7 patients. This procedure was combined with pericarotid and perivertebral sympathectomy in 13 patients. Operation was homolateral on the side of the cerebral lesion in 5 patients and bilateral in 15.

A roentgenologic diagnosis was made in all the patients. It was frequently necessary to establish the presence of intrapleural air when the diagnosis was doubtful. A history of previous attack was obtained from 39 patients (34.2%). Five patients had a recurrence of pneumothorax within the follow-up period, an over-all incidence of 38.5%. Sixty-two patients were treated conservatively with bed rest, minimal activity, and sedation. Eighteen were treated with needle thoracentesis. Twenty-one required the insertion of an intercostal catheter to reexpand the lung, and on 13 a thoracotomy was performed. The surgical procedures included decortication, wedge and segmental resection in patients with localized blebs, and scarification in those with extensive involvement. Three patients, aged 39, 57, and 73 years, respectively, died, representing a mortality rate of 2.6%. Nine patients were discharged from military service, representing a 7% loss of active duty personnel. Spontaneous pneumothorax is a serious, highly recurrent disease; it is a surgical emergency and should be treated vigorously rather than passively.

The Surgical Management of Giant Cavitary Tuberculosis. J. W. Bell. Am. Rev. Tuberc. 77:593-604 (April) 1958 [New York].

The author reports on 30 patients with advanced pulmonary tuberculosis, in whom either unilateral or bilateral giant cavities, 4 cm. or more in diameter, were present. The patients were treated with various combinations of chemotherapy and surgical measures. The surgical procedures consisted of Monaldi drainage alone in 8 patients; a standard 6-to-8-rib thoracoplasty was performed on 10 patients, and subcostal plombage on 5; 4 patients underwent primary resection, and 3 had secondary resection after preliminary Monaldi drainage. No permanent arrest of the disease was obtained in the 8 patients treated with Monaldi drainage alone. In 7 of the remaining 22 patients, the results of thoracoplasty or resection with or without preliminary Monaldi drainage were satisfactory, the disease being converted to an inactive stage. The results obtained are considered indicative of the advanced stage of the disease and of the type of patients with this disease rather than a reflection of the surgical method employed. The most consistent therapeutic results were obtained by thoracoplasty, with disease arrest rates approaching 75% in the prechemotherapy period. Thoracoplasty failures or late relapses after 5-to-10-year intervals, however, now average 10%. The advantages and safety of pulmonary resection, when effective antituberculous drug coverage is available, should make this the treatment of choice. Proceeding on the assumption that nonsurgical treatment will fail in patients with giant cavitary tuberculous lesions, resection may be accomplished within the first 4 to 6 months of original chemotherapy and may result in the greatest possible benefit to the patient, similar to that for all varieties of cavitary tuberculosis.

Pancreatitis. E. T. Bell. Surgery 43:527-537 (April) 1958 [St. Louis].

The first part of the paper is concerned with 179 fatal cases of pancreatitis (100 men and 79 women) observed at autopsy of 61,752 cases (40,328 men and 21,424 women), with 47,518 of the patients over 20 years of age. Only 1 case of pancreatitis was found among 14,234 patients less than 20 years of age. The incidence in men over 20 years of age was 0.25%; in women over 20 it was 0.36%. The ratio of women to men with pancreatitis was about 3 to 2. In men 74% and in women 84% of the cases developed after the age of 40 years. The gross changes in the pancreas noted at autopsy were similar in the acute and chronic cases, except that 20% of the latter showed fibrosis, calcification, or pseudocysts. Death occurred during the first acute attack in 102 of the 179 patients (61 men and 41 women). The symptoms persisted without interruption in 95 cases, but in 7 cases, with a duration of 1 to 3 months, there was temporary improvement followed by an acute exacerbation. Some writers would classify these 7 cases as recurrent pancreatitis. In the 77 patients with chronic pancreatitis (39 men and 38 women), the disease persisted more than 3 months. Sixty-two of these patients had more than 2 acute attacks, that is, they had chronic recurrent pancreatitis, but the remaining 15 patients had continuous abdominal symptoms without any acute exacerbations. The onset was dated from the first attack of abdominal pain, but it is recognized that the first attack in some instances may have been gallstone colic and not pancreatitis. Thirty of the 39 patients with duration of more than 1 year had gallstones. It appears that gallstones are the cause of pancreatitis in about one-third of men and one-half of women over 40 years of age. However, in persons under 40 years of age, alcoholism is more important than cholelithiasis in the etiology of pancreatitis. Thirteen of 32 subjects with pancreatitis in this age group were chronic alcoholics, while only 6 had gallstones. In the literature, 20 to 30% of pancreatitis is attributed to alcoholism. Pancreatic lithiasis is usually a late complication of chronic pancreatitis, but it may develop without signs of pancreatitis.

In the second part of the paper the author comments on the relationship of pancreatitis to diabetes mellitus, citing literature reports and observations on the aforementioned autopsy material. Glycosuria is not often found in patients with mild pancreatitis but is usually present in the later stages of severe pancreatitis. Hyperglycemia of some degree is usually present in all patients with severe pancreatitis. Typical diabetes of short duration often develops in subjects who die several weeks after the onset of an acute attack of pancreatitis. Permanent diabetes finally develops in about 14% of subjects with chronic pancreatitis without lithiasis and in about 45% of those with lithiasis. Acute pancreatitis may develop in a diabetic patient. Only a small percentage of the cases of clinical diabetes are due to pancreatitis (0.38% in the autopsies reviewed). Diabetes due to pancreatitis differs from idiopathic diabetes in the absence of vascular disease, which is so typical of idiopathic diabetes.

Colles' Fractures: Classification and Treatment. E. O. Geckeler and D. J. Gross. Pennsylvania M. J. 61:486-488 (April) 1958 [Harrisburg].

Most of the so-called Colles' fractures are not as simple as they usually are considered. Textbooks fail to emphasize that most of these injuries are not only fractures of the radius but, in a great many instances, are complicated fractures with involvement of the wrist joint. In addition, there may be damage to the pronator quadratus, the flexor tendon sheaths, and the median nerve. In some instances an ischemic condition occurs in the wrist and hand. The injuries, collectively known as Colles' fracture, can be classified as simple (true Colles' fracture), which is stable, and as complicated, which is decidedly unstable. The simple type is a fracture only through the radius, with dorsal tilting of the distal end of the fragment and or slight impaction. There is no damage to the wrist joint. In this form there is little tendency to displacement after reduction; however, the simple type comprises only about 12% of the injuries known as Colles' fracture. In the complicated type the distal end of the radius is comminuted, with shortening, because the cancellous bone structure has been crushed and impacted. In many instances there also is damage to the radioulnar ligament and the triangular ligament, with an avulsion fracture of the ulnar styloid and a lateral shift at the wrist joint. Reduction by manipulation is practically impossible, and deformity will recur after ordinary immobilization. This complicated type comprises approximately 88% of all wrist fractures.

The authors describe their method of treatment of the complicated fracture by traction on the thumb, followed by immobilization in a transfixion cast with 2 Kirschner wires. Traction on the thumb only corrects lateral shifting at the wrist joint and replaces the ulnar styloid when it is fractured. While still in traction, a Kirschner wire is inserted through the metacarpal of the thumb, another wire is inserted through the proximal shaft of the ulna, and the plaster is applied, including the wires, as a transfixion cast. On account of the extensive damage and the tendency to become redisplaced, the transfixion cast must be worn for at least 8 weeks until solid union occurs; then the Kirschner wires are removed, and a light anterior splint is applied, to be worn for 2 additional weeks. The fingers must be exercised frequently during the entire period of treatment, commencing the day after injury; however, function of the fingers is not difficult with such treatment, as the patient is remarkably comfortable and, in most instances, the hand is not decidedly swollen. Approximately 200 complicated, unstable fractures have been treated with this method. A review of the films of 50 unselected cases shows generally satisfactory reduction in every instance, although in some cases of extensive comminution it was not possible to obtain perfect reposition of all fragments. By careful measurements on the x-ray films, it was found that shortening of the radius had been completely corrected in 32 cases or 64%; there was slight shortening in the remainder. Dorsal tilt and lateral shift were entirely corrected in 37 cases or 74%, there being slight residual displacement in the remainder. The final anatomic and functional results were satisfactory except in 2 instances.

Sésamoide Douloureux: Review of Fabella and Affections of Fabella and Personal Case. T. Kjellman. Nord. med. 59:396-398 (March 13) 1958 (In Swedish) [Stockholm].

The fabella is a sesamoid fibrocartilage in the posterolateral part of the knee capsule. It can cause compression symptoms from the knee joint and be the seat of arthrosis deformans, tuberculosis, or fracture. After direct or indirect trauma it can exert a pressure on the peroneal nerve when this is displaced laterally and cause pain in the fabella region and along the course of the peroneal nerve. The condition was described in 1929 by Lepoutre, who called it sésamoide douloureux. In the case reported the condition followed a severe intraarticular fracture of the tibial condyle. Severe pain which persisted after healing of the fracture subsided on extirpation of the fabella.

Villous Adenomas of the Large Intestine: Clinicopathologic Evaluation of 50 Cases of Villous Adenomas with Emphasis on Treatment. M. W. Wheat Jr. and L. V. Ackerman. Ann. Surg. 147:476-487 (April) 1958 [Philadelphia].

The authors report on 25 men and 25 women, between the ages of 33 and 89 years, with villous adenoma of the large intestine, a sessile tumor composed of villi which project above the level of the surrounding intestinal mucosa. The average age of these patients was 62.7 years, and it was exactly the same for men as for women. The most common presenting symptoms were blood and mucus from the rectum or frequent watery stools. In 35 patients the tumor was palpable by rectal examination, and in an additional 9 patients, in whom the tumor could not be palpated, it was visualized by means of the sigmoidoscope. The villous adenomas were located predominantly in the left side of the large intestine, being in the rectosigmoid or distal to it in 41 patients (79%). A total of 49 specimens were taken for biopsy in 35 of the 50 patients. In 26 patients with 37 biopsies, the most significant pathological lesions present were detected by biopsy. However, in the remaining 9 patients on whom 12 biopsies were performed, the most significant pathological lesions were missed. In 16 patients (32%), villous adenomas were associated with other neoplasms (all but 1 of the intestinal tract), which were either benign or malignant. These findings suggest that physical examination should include careful palpation and, if possible, visualization of the adenoma, searching for areas of induration, ulcer, bleeding, and fixation. Multiple biopsies should be performed and carefully oriented for microscopic study. Roentgenographic studies should be carried out and should include an air-contrast type of barium enema specifically looking for additional tumors.

Focal atypical changes were observed in 19 patients; focal carcinoma was found in 13 patients, and carcinoma in 5. Malignant changes thus were found in 37 patients (76%). The adenomas were completely benign in 13 patients. In most of the patients in whom there is no invasive carcinoma, a cure may be obtained by adequate local excision, i. e., removal of the entire villous adenoma in one piece, including the stalk and a margin of normal tissue on all sides including depth. There were 2 postoperative deaths (7.6%) in the group of 29 patients with adequate local excision; of the remaining 27 patients, 13 (48%) are alive without evidence of disease for less than 5 years, and 14 (52%) are alive without evidence of disease for more than 5 years. Treatment of villous adenoma by inadequate local temporizing measures most often leads to repeated local recurrence and occasionally to the patient's [illegible] Irradiation therapy of any type has no place [illegible] the treatment of villous adenomas of the large intestine.

Primary Melanoma of the Esophagus. F. E. Ferro, E. W. Miller, W. A. Morningstar and others. A. M. A. Arch. Surg. 76:492-495 (April) 1958 [Chicago].

The 64-year-old man whose history is presented had had progressive dysphagia, so that now he was able to take only small sips of liquid by mouth, and he had lost 40 lb. (18.1 kg.). A dull ache over the right anterior costal margin had been present for 1 year. Barium swallow showed a dilatation of the proximal part of the esophagus, with narrowing and irregularity of the mucosal pattern of the distal third and a large, well-circumscribed, homogeneous density in that area. Esophagoscopy revealed a dilated upper esophagus and, 28 cm. from the upper gum margin, a necrotic polypoid tumor mass, beyond which examination was not possible. The microscopic report of the biopsy specimen was undifferentiated tumor in necrotic debris. When the right side of the chest was opened, a large tumor mass was visualized, arising in the lower third of the esophagus. An esophagogastrostomy was performed. On the 10th postoperative day the patient could eat without regurgitation, but later the anastomosis separated, and the patient died on the 21st day after the operation. The esophageal tumor measured 11 by 13 by 13 cm. and completely encased the distal third of the esophagus. The overlying pleura formed a pseudocapsule. The tumor was firm on section and showed a mottling of dark brown, black, gray, and yellow. Microscopic examination revealed tumor cells containing melanin pigment. Multiple sections of the esophagus above and below the tumor did not show any junctional tumor foci. No other tumor or pigmented focus was found in the skin, subungual regions, anus, or meninges. Primary melanoma of the esophagus is rare. The case presented brings to 19 the total number reported.

GYNECOLOGY & OBSTETRICS

Technique and Experience with Transabdominal Amniocentesis in 50 Normal Patients. H. M. Parrish, M. E. Rountree and F. R. Lock. Am. J. Obst. & Gynec. 75:724-727 (April) 1958 [St. Louis].

The term "transabdominal amniocentesis" is descriptive of the procedure and is suggested in lieu of previous terminology, including amniotomy, abdominal paracentesis, abdominal aspiration of amniotic fluid, transcutaneous amniotic puncture, and paracentesis uteri. The authors developed their technique for this procedure when amniotic fluid specimens were needed for another study. Amniotic fluid may be obtained for study by 1 of the following methods: (1) by vaginal amniotomy through the cervical os (rupturing the membranes); (2) by vaginal amniotomy, with insertion of the needle either anterior or posterior to the cervix; (3) by transuterine amniotomy at the time of hysterotomy or cesarean section; (4) from intact ova sacs passed at the time of abortion; and (5) by transabdominal amniocentesis. The obvious advantages of the abdominal approach, in preference to the other methods, are as follows: Amniotic fluid can be obtained during any period of gestation after 20 weeks; fluid may be obtained throughout various stages of pregnancy; sterile technique can be more readily enforced; the amount of fluid desired can be easily controlled, and there is minimal leakage from the puncture site; and there is less chance of inducing premature labor with the use of the abdominal approach. Transabdominal amniocentesis was used on 50 clinic patients at the North Carolina Baptist Hospital. With the exception of 3 hospitalized patients in labor, all these procedures were performed on prenatal patients in the outpatient clinic. No patient with previous abdominal or pelvic surgery was included in this study because of the possibility of adhesions binding the intestines to the anterior uterine wall. Patients with medical or obstetric complications of pregnancy were also excluded from this study. None of these patients had clinical evidence of polyhydramnios.

The puncture site which uniformly gave the best results was in the midline half the distance between the umbilicus and the symphysis pubis. When the top of the gravid uterus was below the umbilicus, the puncture site was slightly lower. Novocain was infiltrated down to the peritoneum, and in half of the patients only an intradermal wheal was used. There was no appreciable difference in the response to pain in the 2 groups. A 3½-in.-long, 18-gauge spinal needle with a trocar was then quickly thrust through the skin, abdominal wall, peritoneum, and uterus into the amniotic cavity. Usually, as the needle enters the amniotic sac, the fetus begins to move vigorously, knocking against the needle and causing it to move from side to side. This is not an indication for withdrawal of the needle. Occasionally, a few drops of blood drain from the needle as it pierces the uterine wall or placenta. Forty-six of the 50 transabdominal amniocenteses attempted were successful. No serious maternal or fetal complications resulted directly from transabdominal amniocentesis in 50 patients. The authors conclude that this procedure provides an experimental, diagnostic, and therapeutic means of studying amniotic fluid.

Epidermoid Carcinoma of the Vulva: An Analysis of 238 Cases: Part II. Therapy and End Results. T. H. Green Jr., H. Ulfelder and J. V. Meigs. Am. J. Obst. & Gynec. 75:848-864 (April) 1958 [St. Louis].

In the first of 2 papers on epidermoid carcinoma of the vulva, the authors point out that until fairly recently cancer of the vulva has been one of the most poorly managed malignant lesions. Delay in diagnosis, together with failure to take proper cognizance of the biological nature and mode of spread of the tumor in planning therapy, has resulted in a disappointingly low cure rate. Seeking to evaluate their own efforts, as well as to ascertain whether a trend toward improvement had resulted from more recent advances in surgical therapy, the authors reviewed the experience of the past 25 years at the Vincent Memorial Hospital and the Massachusetts State Department of Public Health Hospital at Pondville. In summarizing the lessons learned or reemphasized by study of the disease and the results of its treatment in 238 patients with epidermoid carcinoma of the vulva from 1927 to 1956, the following points are stressed in the second of the 2 papers: 1. Cancer of the vulva is far more curable by surgery than was formerly realized. In spite of their advanced age and frequently associated obesity, diabetes, and cardiovascular disease, surgery of the magnitude necessary to offer optimum chance for cure is tolerated well by these patients. 2. Leukoplakia is an extremely important precursor of malignant change in the vulva, and a prior syphilitic infection also may be of significance in patients in the younger age group and particularly in Negro women. Certain systemic characteristics of these patients suggest a possible steroid hormone or metabolic disturbance in the etiological background. 3. Radiation therapy offers little; surgery is the treatment of choice. An understanding of the diffuseness and multicentric origins of the primary lesion and an appreciation of the frequency and manner of lymphatic spread are the basis for adequate surgery. Clinical estimation of nodal metastasis is highly inaccurate. Type, microscopic grade, size, and location of the primary lesion have some influence on incidence and distribution of lymph node metastases, but as regards curability these factors are of less significance than an adequate operation. Previous inadequate treatment may complicate the problem but should not alter the basic plan of surgical attack and does not seem to diminish significantly the potential curability. 4. The ideal operation is a radical vulvectomy with dissection in continuity of the superficial and deep nodes of the groins and pelvis. Procedures short of this will not yield satisfactory results. Recent use of a lower abdominal crescent incision in combination with a radical vulvectomy exposure has permitted a safe, effective, 1-stage, en-bloc resection and represents a technical advance. 5. More radical pelvic operations should be considered in selected patients with large lesions and local extension beyond the vulva, if results in this group are to be improved. Posterior pelvic exenteration, if it permits adequate resection of the local disease, can be carried out with a reasonably good chance of cure. 6. Recognition and proper treatment of the almost universal precursor, leukoplakia, and efforts to diminish long delays in diagnosis and treatment will perhaps improve the control of this disease.

Heroin Addiction Among Pregnant Women and Their Newborn Babies. S. O. Krause, P. M. Murray, J. B. Holmes and R. E. Burch. Am. J. Obst. & Gynec. 75:754-758 (April) 1958 [St. Louis].

The authors report observations on 18 women who were acknowledged heroin addicts. Few volunteered the information that they were addicted. Physical examination revealed the characteristic needle puncture marks along the superficial veins of the arms, the hands, and, frequently, the legs. Upon questioning, all admitted their addiction and disclosed the time of their last dose, how often they required the drug, and how long they had been on it. These mothers responded to a sympathetic approach, particularly if assured that their withdrawal symptoms would be treated. Only 4 of the 18 women had received prenatal care. At the time of their hospital admission, 2 patients had preeclampsia; 2 had infected ulcerating veins; 2 were admitted in false labor, and delivery followed 2 weeks later; 1 had a marginal premature separation of the placenta; and 6 had premature labor with or without prematurely ruptured membranes, calculated from a known period of gestation. There were 5 patients who could not give an approximate date of the last menstrual period; 1 of these was delivered of a baby premature by weight, bringing the total cases of premature labor to 7, or 39%.

Withdrawal symptoms appeared in 16 of the patients from 6 to 24 hours after delivery. A few showed only mild nervousness and insomnia, but most of them had tremors and severe anxiety with crying. Four mothers left the hospital against advice within the first 48 hours. The 12 mothers who had withdrawal symptoms and did not sign out all responded favorably to methadone in doses of 5 to 10 mg. None appeared to need the methadone for longer than 3 days, but it is impossible to know how many were being supplied heroin from the outside. It is assumed that the 2 women in whom withdrawal symptoms did not develop after delivery were supplied with heroin from outside the hospital.

Withdrawal symptoms developed within 1 to 56 hours after birth in 15 of the 18 babies. They presented a fairly characteristic syndrome: An excess of mucus interferes with respiration and necessitates repeated aspiration and administration of oxygen. Within 6 to 18 hours, and occasionally earlier, an abnormal tremor of the arms and legs is noted. This heralds the advent of vomiting and the inability to nurse. Many of these babies, when given the bottle, seem to have difficulty swallowing. Respiratory crisis and cyanosis may occur at this time. Vomiting begins within 24 to 36 hours; it may be mild and last only 2 to 3 days or may be so severe that no formula or water is retained for 5 to 6 days. The babies that survive are usually asymptomatic within 6 to 7 days. Barbiturates, belladonna, paregoric, and special formulas seem to have no value in their management. Four babies in this series died between the 6th and 18th days. One of these deaths might be attributed to anomalies incompatible with life, but the baby exhibited all the above symptoms. These babies were apathetic and emaciated, and all appeared to die of respiratory distress. The authors prevailed upon the pediatric department to treat the babies for withdrawal symptoms of heroin addiction, and methadone was given in doses of 0.5 mg. every 4 to 12 hours. This regimen was started within the first 24 hours and continued in decreasing doses. The 5 babies so treated survived and had less severe symptoms for a shorter period than those treated symptomatically.

PEDIATRICS

Failure of Penicillin and Sulfonamide to Prevent Beta-Hemolytic Streptococcal Infections: Sibling Prophylaxis of Streptococcal Infection. B. B. Breese and F. A. Disney. A. M. A. J. Dis. Child. 95:359-363 (April) 1958 [Chicago].

Four hundred thirty-one sibling contacts of 257 children with bacteriologically proved streptococcic infections were given prophylactic treatment. Of the 431 children, 150 received 1 tablet of 200,000 units of benzathine penicillin G (Bicillin) daily, 166 were given 1 tablet of 0.5 Gm. of sulfadiazine, and 115 received a placebo. Each preparation was given for 5 days. Whenever possible, a throat culture was obtained on all contacts before the use of prophylaxis. Five days after the completion of the prophylaxis, cultures were taken on the child with primary streptococcic disease and on all sibling contacts. Of 151 contacts who were found to be negative before they received prophylactic treatment, 15 were subsequently found to have positive cultures, and 10 of these were ill. In 9 of the 15 it was possible to compare the type of Streptococcus organisms found in the patient with the primary disease and in the contact. In only 1 case was the type the same. No statistically significant difference could be demonstrated in the attack rate of streptococcic infection among the various prophylactic groups. Among the 234 contacts on whom throat cultures could not be obtained before the use of prophylaxis, 35 were subsequently found to be positive for hemolytic streptococci, and 11 of these were ill. In these contacts, also, no statistically significant differences could be demonstrated in the incidence of streptococcic infections in those given different prophylactic agents. In 5 cases it was possible to compare the type of Streptococcus organisms found in the patient with the primary disease and in the contact. In only 1 instance was the type the same.

These data suggest that little is to be gained by prophylaxis of siblings of children with primary streptococcic infections. Moreover, these observations would seem to indicate that probably a high proportion of infections in siblings occur before prophylaxis can be given to them. Failure of prophylaxis in siblings of children with primary streptococcic infections contrasts with the excellent results of prophylaxis in rheumatic patients and military groups given continuous prophylaxis with either the sulfonamides or penicillin preparations. Instead of giving sibling contacts of children with primary streptococcic disease small doses of prophylactic agents, it seems wiser to watch for illness in the siblings and then give full therapeutic dosage. As for carriers or unrecognized cases in the family, unless cultures are taken, these will be missed in many cases. In the absence of culture a sibling with the story of a mild "sore throat" should be suspected of being a carrier and be given therapy rather than prophylaxis to eliminate the Streptococcus organisms.

Renal Vein Thrombosis: 1. Age Incidence in Infancy and Childhood; 2. Sex Incidence; 3. Incidence of Unilateral and Bilateral Involvement. H. J. Kaufmann. A. M. A. J. Dis. Child. 95:377-384 (April) 1958 [Chicago].

The author reports the case of a 1-year-old girl with thrombosis of the renal vein, who was admitted to the pediatric service of the Boston City Hospital with the chief complaint of fever, irritability, and an attack of vomiting of 12 hours' duration. The urine was yellow and acid, with albumin 2+ and sugar 2+. There were numerous red blood cells per high-power field and occasional white blood cells. The sediment was loaded with bacteria, granular casts, and crystals. The nonprotein nitrogen value had risen to 68 mg. per 100 cc. An intravenous pyelogram showed absence of dye in the right kidney. Cystoscopy yielded no urine from the right side. Retrograde pyelography showed a normal left ureter and kidney, but there was a block from the midureter upward on the right. These findings appeared to make a diagnosis of thrombosis of the renal vein most likely. Through a right-sided lumbar incision, thrombosis of the right renal vein and adrenal vein was found, together with an enlarged hemorrhagic kidney. The right kidney and adrenal were removed. Six months after discharge the infant showed excellent progress with normal growth and development. A review of 96 cases of renal vein thrombosis in children, collected from the world literature since 1900, revealed that 38 (40%) occurred in infants over 2 months of age. No significant difference in sex distribution was found. In boys, renal vein thrombosis was found with essentially equal frequency on the right side, on the left side, and bilaterally. In girls, bilateral thrombosis occurred most frequently; unilateral thrombosis was found much oftener on the left than on the right side. At present there is no explanation for these differences in occurrence.

Addison's Disease in Three Six-Year-Old Boys. B. M. Malloy and C. W. Woodruff. A. M. A. J. Dis. Child. 95:364-369 (April) 1958 [Chicago].

The authors report on 3 6-year-old boys with Addison's disease. The first of the 3 patients also had hypoparathyroidism and moniliasis, with adrenal crises being the presenting endocrinopathy. All 3 were in adrenal crisis when first seen and responded rapidly to parenteral therapy with cortisone or its derivatives, sodium chloride, and dextrose and water. In none of them was pituitary failure suspected on clinical grounds. In the first patient, the physicians' attempt to educate his family concerning the need for medical care at the onset of any illness proved inadequate. The availability of parenteral replacement therapy in his parents' home, where he died, might have saved the boy's life. The erythrocyte cation observations made in this patient are reported because no similar observations in children were found in the literature. Compared with the first sample, red blood cell sodium decreased to imperceptible levels at 41 hours. Increases from 41 to 113 hours and from 113 to 161 hours were observed. An increase in the level of red blood cell potassium from zero to 41 and from 41 to 113 hours was also found. The decrease in erythrocyte sodium after cortisone administration was in accordance with the observations by other workers. The significance of the increase in red blood cell sodium and the slight absolute decrease in red blood cell potassium at 161 hours was not clear. In the preceding 24 hours, cortisone maintenance therapy had been decreased from 50 to 25 mg. daily. These changes may have been associated with relative adrenal insufficiency incidental to the decrease in cortisone administration. The other 2 boys were maintained in good health on replacement therapy with cortisone, fludrocortisone, and sodium chloride administered by mouth.

Since 5 of 12 patients, aged 10 years or younger, with Addison's disease, whose cases were collected from the literature, had hypoparathyroidism and/or moniliasis or had a sibling with this combination of diseases, it should be looked for in all children of this age with Addison's disease. Similarly, patients with hypoparathyroidism should be watched for the development of adrenal insufficiency. The rapidity of onset of adrenal crisis in this age group makes early recognition of this disease a challenge.

Etiologic Factors in Cerebral Palsy and Their Correlation with Various Clinical Entities. S. Brandt and V. Westergaard-Nielsen. Danish M. Bull. 5:47-52 (Feb.) 1958 (In English) [Copenhagen].

The authors studied 628 cases of cerebral palsy. Prenatal factors, including prematurity, were found to be responsible for a comparatively large group of spastic diplegia cases, and the correlation was even higher for cases of symmetric diplegia and paraplegia than for those of asymmetric diplegia. Postnatal factors were found in 32% of the patients with left hemiplegia and in 16% of those with right hemiplegia. In many cases the histories gave no suggestion of etiology. There are cases where 2 or more factors may each be more or less responsible of renal origin. The actual mechanism producing these manifestations is not clear from the findings in this investigation.

THERAPEUTICS

Application of the Newer Corticosteroids to Augment Diuresis in Congestive Heart Failure. A. D. Riemer. Am. J. Cardiol. 1:488-496 (April) 1958 [New York].

Early clinical investigations with prednisone (Meticorten) in 13 patients, between the ages of 19 and 79 years, in whom the use of this drug was indicated primarily for noncardiac conditions, such as rheumatoid arthritis, status asthmaticus, silicosis, and pemphigus, revealed significant diuresis in 11 of the 13 patients who had coexisting heart disease with edema. The diuretic effect occurred within 4 to 7 days after the administration of prednisone was started. These findings induced the author to add administration of prednisone to the intensive, but no longer effective, therapy of a 47-year-old man with coronary sclerosis, multiple myocardial infarcts, and refractory anasarca. There followed an immediate restoration of response to diuretic drugs with rapid loss of edema and full restoration of compensation. This was maintained for 13 months despite diminished intensity of all other cardiac therapy. Finally sudden chaotic rhythm and death occurred. Autopsy did not reveal any evidence of venous congestion or edema.

Prednisone then was added to the treatment of resistant cardiac edema in 8 additional patients, between the ages of 47 and 83 years, who also had no established need for the administration of corticosteroids. All of them had received prolonged, but occasionally ineffective, treatment with digitalis and diuretic drugs. After the addition of steroid administration to the treatment, 7 of the 8 patients had prompt diuresis and improvement of cardiac function. Glycosuria did not occur in any of these patients to aid increase of water output. Especially important was the continued use of diuretics and the employment of small doses of prednisone. In the 7 patients, the efficacy of mercurials or acetazolamide was so intensified that the use of either was followed by marked diuresis on the first day of the new regimen. This was in contrast to the onset of diuresis in the first 13 patients in whom the diuretic effect was slightly delayed. Similar augmentation of diuresis followed the use of prednisone in an additional 9 patients, 6 of whom had decompensated rheumatic heart disease and 3 had decompensated asthmatic cor pulmonale.

Several mechanisms seem to be involved in the potentiality of adrenal steroids for aiding diuresis in patients with congestive heart failure. Most important appear to be the interrelated actions which alter physicochemical activities in the nephron, especially the repotentiation of diuretic drugs and possibly the suppression of "secondary aldosteronism." This specific diuretic function may be additive to the anti-inflammatory action by steroids in patients with decompensated rheumatic heart disease or decompensated cor pulmonale of pulmonary fibrosis. Routine use of adrenal steroids in the treatment of cardiac edema is not at present being advocated. Only when the standard measures, particularly the use of digitalis, proper administration of diuretic drugs, and correction of electrolyte imbalance, occasionally fail, the addition of corticosteroids may be considered. For clinical application there are as yet no established pharmaceutical standards for dosage, time of day, and duration of administering the corticosteroids. Also, the treatment is occasionally unsuccessful, and attempted explanations for this are not yet conclusive. There must be the usual precautions regarding associated disorders, such as peptic ulcer, tuberculosis, and infections in general. If steroids are used, it is urged that all basic cardiac therapy be continued, especially the administration of diuretic drugs which may become immediately effective.

Laboratory and Clinical Observations on Ethoxzolamide (Cardrase) as a Diuretic Agent. J. H. Moyer and R. V. Ford. Am. J. Cardiol. 1:497-504 (April) 1958 [New York].

Diuretic bioassay studies were carried out on 10 patients in mild heart failure, who were given ethoxzolamide (Cardrase) (6-ethoxybenzothiazole 2-sulfonamide), a carbonic anhydrase inhibitor, for 2 successive days. The minimum dose administered was 31.75 mg. The maximum dose used was 500 mg., given as a single dose in the morning. The patients drank 3,000 cc. of distilled water per 24 hours and consumed a diet containing 50 mEq. of sodium per 24 hours. After the dose of the drug was established which produced maximum natruresis in most of the patients, a dose of at least 2 times this dose at the apex, i. e., 250 mg., was given as the comparative testing dose of ethoxzolamide for the bioassay studies. The response was then compared to that obtained with a daily dose of 250 mg. of acetazolamide (Diamox). A second group of 13 ambulatory patients, between the ages of 48 and 73 years, with various degrees of cardiac failure were given 500 mg. of ethoxzolamide daily in 2 divided doses for 5 consecutive days out of each of 2 weeks. The patients returned semiweekly for evaluation while receiving this dose. On the 14th day the dose was increased to 1,000 mg. daily in 4 divided doses administered for an additional 2 weeks. The patients were seen for evaluation at least semiweekly while receiving the high dose.

Results showed that ethoxzolamide is equally as potent as acetazolamide, which also acts by inhibition of carbonic anhydrase, in its ability to increase water and sodium excretion. The diuretic-toxic range of ethoxzolamide is more narrow than that of acetazolamide. Two of the 10 patients in the first group had undesirable side-effects after the administration of 250 mg. of ethoxzolamide daily for 2 days; 1 patient complained of paresthesias about the mouth, weakness, and lethargy; and the other complained of weakness and lethargy. Side-effects were not observed when a dose of 125 mg. was given to 6 of these 10 patients for 2 days. Discontinuation of the administration of ethoxzolamide was required in 2 of the 13 patients receiving 500 mg. daily for 2 weeks, because of diarrhea, paresthesias, fatigue, weakness, and leg cramps in 1 patient and because of abdominal cramps and diarrhea in the other. The common side-effects with the 500-mg. dose were lethargy and weakness in 8 patients, paresthesias in 2 patients, anorexia in 3 patients, intestinal cramps and diarrhea in 6 patients, and dizziness in 2 patients. Therefore, the smallest dose which will produce maximum diuresis should always be used. The bioassay studies showed that a dose of 125 mg. per day produces nearly maximum diuresis. With this dose side-effects are minimal and are no more severe than those observed with the administration of acetazolamide. There is certainly no need for a dose in excess of 250 mg. of ethoxzolamide per day, and this appears to be the maximal dose of the drug which should be used.

The Effectiveness of Rolicton, A New Oral Diuretic, in Severe Cardiac Failure. I. R. Callen. Am. J. Cardiol. 1:511-513 (April) 1958 [New York].

A proprietary preparation of aminoisometradine, Rolicton (1-methallyl-3-methyl-6-aminotetrahydropyrimidinedione), was given a therapeutic trial as a diuretic in 89 patients, 80 of whom had congestive heart failure, 3 had renal disease, 3 had hepatic disease, and 3 had other disorders. Ten of the 89 patients were gravely ill with severe symptoms and extreme cardiac failure, and 79 had mild to moderate edema or congestive failure. Nineteen patients were hospitalized, and 70 were outpatients. The drug was available in tablets of 400 mg., and dosages of 600 to 2,400 mg. were given daily. Sixty-four patients (72%) obtained excellent or good results, 13 patients (15%) obtained fair results, and 12 (13%) were therapeutic failures. The greatest dramatic diuretic effect was noted in the 10 patients with severe cardiac failure, 4 of whom had rheumatic cardiovalvular disease, 4 had arteriosclerotic cardiovascular disease, and 2 had hypertensive disease. Eight patients had some side-effects. Two discontinued administration of the drug. Six had nausea, 1 of them stopping the therapy; the other 5 were able to continue the treatment, and the nausea disappeared. These data suggest that aminoisometradine is an effective, well-tolerated, orally administered diuretic that can be tried in refractory cases of cardiac failure in conjunction with other therapy. It appears to have its greatest usefulness for maintenance in patients with mild to moderate degrees of cardiac failure.

Treatment of Early Syphilis with Penicillin. R. R. Willcox, F. J. G. Jefferiss and G. L. M. McElligott. Brit. J. Ven. Dis. 34:14-15 (March) 1958 [London].

Although penicillin in a total dosage of 2.4 mega units (mega unit=1 million units) had been used throughout the British Army and the Royal Air Force for the treatment of primary and secondary syphilis since 1944, in the civil clinics it was at first the common practice to follow a course of 2.4 to 4 mega units of penicillin with 10 weekly injections of neoarsphenamine and bismuth. The authors believe that the idea of consolidation treatment with subcurative doses of arsenic and bismuth is mistaken and that, if any Treponema organisms survive after intensive penicillin treatment, it would be more logical to attack them again with the most efficient treponemicidal agent at one's disposal rather than to administer potentially dangerous drugs in a dosage more likely to be suppressive than curative. The results of the treatment of 864 patients with primary and secondary syphilis at St. Mary's Hospital, London, are reviewed. Of these, 561 received treatment with penicillin and a short course of arsenic and bismuth, 183 were given penicillin and a maximum of 10 injections of bismuth, and 120 received penicillin alone. In the series, as a whole, the clinical and serologic results have been excellent and seem, if anything, to have been better, rather than worse, when penicillin alone was used. This may be explained by the higher doses of penicillin given over a longer period when no adjuvant metallotherapy was given, and by the fact that in more recent years the possibility of reinfection must be greatly diminished. Moreover, when penicillin alone was used, side-effects from treatment were hardly ever encountered. Penicillin alone is confidently recommended as the treatment of choice in early syphilis.

Experimental and Clinical Observations on the Effect of a New Synthetic Ganglionic Blocking Agent: Mecamylamine Hydrochloride. G. Marchetti, S. Nava and A. Tartara. Minerva med. 49: 606-614 (Feb. 21) 1958 (In Italian) [Turin, Italy].

Ganglionic blocking action of mecamylamine was investigated experimentally in animals and clinically in 2 groups of patients with arterial hypertension. Mecamylamine exerted low toxicity in rats. Intravenous administration of varying doses of mecamylamine (0.1 mg., 0.5 mg., and 0.05 mg.) to anesthetized dogs caused a marked decrease in systemic blood pressure; pulmonary arterial blood pressure fell only slightly. Comparison of the hypotensive coronary effect of 1 mg. of mecamylamine and of 10 mg. of pentamethonium was made on the exposed hearts of 20 rabbits. Mecamylamine produced a marked decrease in coronary blood pressure, whereas pentamethonium exerted almost no decrease in pressure. Administration of mecamylamine to 5 rabbits indicated that alteration of cerebral blood pressure follows only passively the changes of the systemic blood pressure, decreasing or increasing when the latter decreased or increased.

Of the patients with arterial hypertension, the first group consisted of 6 patients, aged 43 to 70 years, who were given a single dose of 10 to 15 mg. of mecamylamine. Two patients with essential hypertension derived marked benefit from the drug. Of 2 patients with renal hypertension, 1 did not benefit and the other was worse off from the drug therapy. The second group consisted of 34 patients, aged 43 to 68 years, of whom 20 had the arteriosclerotic type, 9 the essential type, and 5 the renal type of hypertension. Mecamylamine therapy was instituted 1 to 2 weeks after the patients were hospitalized and lasted 8 to 20 days. The initial daily oral dosage of mecamylamine was 5 mg. given in 2 divided doses. Daily dosage was gradually increased until it reached 50 mg. in some patients. Fourteen patients with arteriosclerotic hypertension derived benefit even from small doses of the drug (15 to 30 mg.). The effect in patients with essential hypertension varied; 6 patients responded to the treatment, 1 did not respond, and 2 patients had a sudden drop in peripheral blood pressure. Of 5 patients with renal hypertension, a small decrease in blood pressure took place in 3 patients and no decrease in 2. Side-effects were mild and included constipation, nausea, and throat dryness. Proper regulation of the initial dose of mecamylamine is essential, because even small doses of the drug have produced a sudden drop in blood pressure in some patients.

Antibiotic and Chemotherapeutic Treatment of Tracheobronchial Adenopathy and of the Primary Complex in Infancy. T. Feliciangeli. Minerva pediat. **10**:149-167 (Feb. 18) 1958 (In Italian) [Turin, Italy].

Clinical and roentgenologic progress of the primary complex associated with tracheobronchial adenitis was studied in 111 infants who received either streptomycin or isoniazid or a combination of the 2 drugs. The average daily dosage of streptomycin was 0.04 to 0.05 Gm. per kilogram of body weight administered intramuscularly in 4 divided doses. The average daily dosage of isoniazid was 8 to 10 mg. per kilogram of body weight administered orally in 4 divided doses. Patients were divided into 4 groups according to the stage of the disease. The first group consisted of 35 infants, below 2 years of age, who had the primary complex. They received the antibiotic treatment for a period of 8 to 55 days. Combined drug therapy gave better results than single drug therapy. Clinical improvement, including gain in weight, greater vivacity, and normalization of body temperature, was observed within 8 to 15 days of treatment. Roentgenologic improvement of the disease was observed between the 4th and the 8th month, being more rapid in patients who received chemotherapy for a longer period of time. Lesions of the primary complex have healed by fibrosis and calcification within 6 to 7 months in infants who were given chemotherapy for a period of 40 to 60 days; healing took place within 10 to 13 months in infants who received chemotherapy for a period of 8 to 20 days. The second group consisted of 57 infants and children, between the ages of 3 months and 12 years, who had a primary complex and tracheobronchial adenopathy accompanied by an extensive exudative process. Chemotherapy brought about clinical improvement within 15 to 20 days of drug administration. Roentgenologic improvement developed more slowly. Small perifocal infiltrations regressed within 30 to 40 days, whereas the extensive ones regressed within 3 to 6 months. There was no great difference in therapeutic effect between streptomycin and isoniazid, but better results were obtained with a combined than with a single drug therapy. Pleural lesions regressed more rapidly (in about 40 days) than parenchymal lesions accompanied by the exudative process.

The third group of patients consisted of 4 infants, aged 11 to 24 months, who had a primary complex followed by progression of the tuberculous lesions. They were given a combined streptomycin-isoniazid therapy for 5 to 8 months. This therapy could not stop the progression of the tuberculous lesions, because it was begun a month after the clinical disease appeared. Two of these infants received collapse therapy. Clinical improvement was observed during the first few weeks, and roentgenologic improvement was noted, beginning the 5th month of chemotherapy. The fourth group consisted of 15 children, aged 6 to 12 years, who have had active hilar adenopathy. Drug treatment lasted 10 to 40 days. Roentgenologic improvement followed the improvement in the general condition. Healing of the lesions in the lymph nodes was noted after 7 to 12 months of drug medication. Isoniazid produced more rapid effect than streptomycin. The author concludes that chemotherapy was effective in all stages of infancy and childhood in this series of patients and was more efficacious in infants below the age of 2 years than in those older. Combined therapy was particularly effective in those types of tuberculosis which were accompanied by the exudative process.

Is the Hargraves Cell Really Specific for Acute Disseminated Lupus Erythematosus? F. Siguier, C. Bétourné, J. Badin and J. Bonnet de la Tour. Semaine hôp. Paris 34:768-773 (March 18) 1958 (In French) [Paris].

Modern methods of investigation have made it possible to detect L. E. (Hargraves) cells in more than 80% of patients with acute disseminated lupus erythematosus. Some of the patients in whom L. E. cells cannot be found, however, present such a characteristic picture of malignant visceral lupus erythematosus that the diagnosis cannot be questioned. Inability to discover L. E. cells in cases of this kind does not really detract from the diagnostic value of the L. E. cell, however, because it is offset by such findings as (1) the appearance of L. E. cells coinciding with the transformation of chronic lupus erythematosus into acute disseminated lupus erythematosus; (2) the persistence of L. E. cells in cases of malignant visceral lupus erythematosus which has apparently become quiescent after a spontaneous remission in the clinical symptoms; (3) the inability of hormone therapy to bring about the disappearance of L. E. cells even though it has a dramatic effect on elements of the clinical picture; and (4) the transient appearance of L. E. cells in a clinically healthy infant whose mother had acute disseminated lupus erythematosus. Further support for the diagnostic significance of the L. E. cell is provided by the extreme rarity with which it appears in the other collagen diseases with the exception of chronic progressive polyarthritis.

Recent investigations, on the other hand, have revealed the presence of L. E. cells in an increasing number of patients with chronic progressive polyarthritis (27% of cases in the latest statistics) and also in patients with certain diseases due to autoimmunization; in those with conditions accompanied by hypergammaglobulinemia; and in those with disorders attributable to hypersensitization. These findings, although they do not expressly contradict the specificity of the L. E. cell, seem to some extent to reduce its value as a diagnostic indicator. The problem has lately been further intensified by reports of cases in which the administration—experimental or therapeutic—of hydralazine has been followed by the appearance of genuine acute disseminated lupus erythematosus.

Hydralazine-Induced Lupus Erythematosus. F. Siguier, C. Bétourné and J. Bonnet de la Tour. Semaine hôp. Paris 34:773-784 (March 18) 1958 (In French) [Paris].

Hydralazine-induced lupus erythematosus is a new post-treatment syndrome originally reported in 1953 by American authors. The first French case appears to have been the one presented by the authors to the Medical Society of the Hospitals of Paris in November, 1957. The patient, a 49-year-old man, whose history was noncontributory, first sought the advice of other physicians because of persistent headache. He was found to have an arterial pressure of 220/130 mm. Hg. Several methods of treatment were tried without success, but at last a consultant suggested the regular use of hydralazine (Apresoline) hydrochloride in a daily dose of 300 to 350 mg. The patient was examined every 3 months at first, and a definite improvement was noted in his condition. The pressure readings were regularly less than 200 for the systolic and did not exceed 100 for the diastolic. He was advised to stop taking Apresoline after he had taken it uninterruptedly for 9 months, but instead of doing so he kept on with it for another 6 months. He then began to have violent pains in his ankles, knees, wrists, and finger joints, with fever, anorexia, chills, and general malaise. He lost 6 kg. (13 lb.) in a few weeks, and 2 months after the onset of these disturbances the characteristic butterfly rash appeared. A diagnosis of acute disseminated lupus erythematosus was made, and the prognosis was believed to be very poor. The authors were then consulted. The patient's general condition, although impaired, did not seem to them to be alarming, but he was found to have anemia, leukopenia, and hypergammaglobulinemia, with a few characteristic L. E. cells. The connection between the prolonged hydralazine treatment and the acute lupus erythematosus-like syndrome seemed perfectly clear. The authors, however, had great difficulty not only in persuading the patient to discontinue the treatment but also in convincing his family of a favorable prognosis. The withdrawal of Apresoline, without any other therapeutic measure, was followed in 4 weeks by a reduction in fever, improvement in the general condition, and finally disappearance of the joint pains and the eruption. Leukopenia disappeared in 6 weeks, anemia in 8, and 3 months after the patient stopped taking Apresoline L. E. cells could no longer be found in his blood. Even more convincing proof of the connection between Apresoline and the lupus erythematosus-like syndrome was provided when the patient, disturbed about 3 months later by the return of headache and an increase in his blood pressure to its former high levels, began taking Apresoline again in the same doses as before. He did this on the advice of his other physicians, who, like himself, were skeptical of the authors' diagnosis. This second course of Apresoline led 8 weeks later to the same symptoms of pain, fever, impairment of general condition, and even the same facial eruption. The patient, convinced by this recurrence, quickly gave up the hydralazine treatment and within a fortnight the syndrome was gone, not to reappear.

The circumstances in which this hydralazine-induced lupus erythematosus appears seem to be independent of a specific allergic terrain or a specific type of hypertension; apparently it is caused only by large doses of hydralazine taken for prolonged periods. The most important characteristic of the induced syndrome is that it regresses when the causative drug is withdrawn and recurs when its administration is begun again. Attempts were made by the authors to reproduce the syndrome by administering hydralazine to guinea pigs; in 10 of the animals L. E. cells appeared in the blood, and the accompanying disease proved fatal in from 2 to 4 months. The best explanation of the drug-induced syndrome seems to be that the combination of hydralazine with proteins produces an antigenic complex, which, in turn, leads to the formation of specific antibodies. The resulting antigen-antibody conflict would explain the rapid clinical relapses that take place in patients sensitized by previous treatment when the administration of the drug is resumed.

Bleeding from the Upper Part of the Gastrointestinal Tract Secondary to Ingestion of Acetylsalicylic Acid (Aspirin). T. A. Lamphier and W. A. Young. J. Internat. Coll. Surgeons 29:395-401 (April) 1958 [Chicago].

The authors report on 12 patients with hemorrhage from the upper gastrointestinal tract secondary to the ingestion of aspirin, in whom microscopic evidence of mucosal irritation was present in the form of acute gastritis. The mucosa was congested and edematous with flakes of adherent mucus containing aspirin fragments and often altered blood. Multiple erosions were visible to the naked eye in 5 patients and microscopically in all. Histologically, polymorphonuclear and round-cell infiltration was observed together with the glandular erosion. The picture was typical of acute gastritis. In 3 specimens in which the reaction was severe, the aspirin left in the stomach was in large sections, and the mucosal reaction was noticeably poor. There was no recurrence of gastric hemorrhage in any of the patients, once the causative factor became known and the use of aspirin was discontinued. In 6 of these patients the condition was apparently the result of prolonged aspirin therapy. The other 6 patients were considered true examples of hypersensitivity. There are two types of reaction in patients with sensitivity to aspirin: (1) alterations in the prothrombin level and (2) depletion of ascorbic acid stores with subsequent increased capillary fragility and lack of adhesiveness of platelets. Hypersensitivity to aspirin should be considered in the differential diagnosis of bleeding from the upper part of the gastrointestinal tract. Emergency subtotal gastrectomy can and should be avoided when aspirin is known to be the causative factor. Emphasis is placed on hypoprothrombinemia as the actual chemical and therapeutic relation of sweet clover disease in animals and bleeding from the upper part of the gastrointestinal tract caused by aspirin in man.

Hypoglycemic Actions of Phenethyl-Amyl- and Isoamyl-Diguanide. R. H. Williams, D. C. Tanner and W. D. Odell. Diabetes 7:87-92 (March-April) 1958 [New York].

Experiments made on guinea pigs suggested that phenethyldiguanide lowers the blood sugar level by (1) promoting anaerobic glycolysis, with increased glucose utilization, and (2) causing decreased gluconeogenesis, with a decrease of the output of glucose from the liver. Preliminary observations are reported which were made on 66 patients with diabetes mellitus who were treated with hypoglycemic diguanide compounds. Twenty-six patients were given phenethyldiguanide; 25, amyldiguanide; and 15, isoamyldiguanide. Each of the 3 drugs used appeared preferable to tolbutamide or insulin in some patients. Nausea and/or vomiting occurred relatively frequently, and, when they did, discontinuation of the diguanide therapy might be indicated. No other significant untoward reactions to these drugs were observed. Some patients did not have side-effects despite the administration of large doses. Results obtained with isoamyldiguanide appeared to be less satisfactory than those obtained with the other 2 diguanide compounds. More extensive studies will be required to determine the net usefulness, as well as the hazards, of this type of therapy.

PATHOLOGY

Mediastinal Granulomas: A Revised Concept of Their Incidence and Etiology. J. W. Peabody Jr., R. B. Brown, M. B. Sullivan and A. Cannon. J. Thoracic Surg. 35:384-396 (March) 1958 [St. Louis].

Of 37 patients with primary mediastinal tumors, operated on at the National Naval Medical Center in Bethesda, Md., in the last 10 years, 12 patients, 7 men and 5 women, between the ages of 19 and 36 years, had granulomas, a relative incidence far higher than that generally ascribed to mediastinal granulomas. Noteworthy features in this group of 12 patients included a low percentage of correct preoperative diagnoses, a uniformly negative bacteriological yield in those cases in which the granulomatous contents were cultured, the frequency with which the pathologist mistook the lesion for some totally different tumor, such as cystic teratoma or bronchogenic cyst, the remarkably high incidence of strongly positive histoplasmin reactors (5 of the 12 patients), and a routine failure to establish a specific cause other than that in 1 patient in whom acid-fast bacilli were supposed to have been demonstrated. Microscopic examination of the removed granulomas with the aid of the periodic acid-Schiff stain revealed Histoplasma capsulatum in 4 specimens. In 1 of the 4 granulomas the fungus was present in abundance, while in the other 3 the visualization of diagnostic forms required persistent microscopic search. In still another case, H. capsulatum was found only after resorting to Gomori's methenamine-silver nitrate stain. Microscopic examination of 2 other granulomas removed from patients with strongly positive reactions to the histoplasmin skin test and negative reactions to the tuberculin skin test was negative for the fungus, as was that of the remaining 5 mediastinal granulomas. These findings suggest that histoplasmosis is more commonly the cause of mediastinal granulomas than has previously been thought.

Sequelae of Arteriosclerosis of the Aorta and Coronary Arteries: A Statistical Study in Diabetes Mellitus. S. Goldenberg, M. Alex and H. T. Blumenthal. Diabetes 7:98-108 (March-April) 1958 [New York].

The authors studied the effects of diabetes mellitus on the sequelae of arteriosclerosis of the aorta and coronary arteries in 1,967 men and 1,503 women who died at the Jewish Hospital in St. Louis and on whom autopsies were performed over a period of about 30 years. Of the 3,470 patients, 264 (7.6%) had diabetes and 3,206 did not. Of the 3,206 nondiabetic patients, 1,842 (57.5%) were men and 1,364 (42.5%) were women, while of the 264 diabetics, 125 (47.3%) were men and 139 (52.7%) were women. The women thus predominated in the diabetic group, and the men in the nondiabetic group. Hypertension was almost twice as frequent among diabetics as among nondiabetics. It was more frequent among nondiabetic men than women, and it was about equally frequent in the 2 sexes among diabetics. Myocardial infarction was also about twice as frequent among diabetics as among nondiabetics. In the latter group the ratio of men to women was 1.8 to 1, compared with 1.3 to 1 among diabetics. About 50% of the nondiabetic men with hypertension, as compared with about 75% of the diabetic men with hypertension, had myocardial infarction, or an increase in the latter group of about 25%; about 33% of the nondiabetic women with hypertension, as compared with 60% of the diabetic women with hypertension, had myocardial infarction, or an increase in the latter group of about 27%. The loss of male predominance to myocardial infarction in older age groups among nondiabetics was associated with an increasing incidence of hypertension among women of more advanced age and a diminishing difference in the incidence of hypertension between men and women. In patients without hypertension there was no significant difference in the incidence of myocardial infarction between diabetics and nondiabetics. In the nondiabetic group the ratio of men to women was 1.3 to 1 as compared with 1 to 1 in diabetics.

The average age at death in the diabetic group was 2.5 years greater than in the nondiabetic group. In the nondiabetic group men lived, on the average, 1.1 years longer than women, while in the diabetic group there was no significant difference between the 2 sexes. There was no significant difference between the 2 groups in the average age at death of patients in whom myocardial infarcts were found at autopsy. However, in the nondiabetic group women lived on the average 5 years longer than men, while in the diabetic group the average age at death was identical in the 2 sexes. While there was no significant difference between the 2 groups with respect to the recovery rate from an initial infarct, diabetics showed an almost 15% higher incidence of subsequent acute infarction from which they succumbed. Correspondingly, nondiabetics who recovered from an initial infarct showed a greater tendency to succumb to cerebrovascular sequelae or myocardial failure than diabetics. The incidence of myocardial rupture after transmural infarction was twice as high among diabetics as among nondiabetics, while the reverse was found in the incidence of development of ventricular aneurysm after healing of a transmural infarct. There was no significant difference between the 2 groups as regards the incidence of development of arteriosclerotic aneurysms or cerebrovascular sequelae. However, the incidence of the phenomenon of atheromatous embolization was over 3 times as high in diabetics as in nondiabetics.

These data indicate that the increased susceptibility to coronary heart disease in diabetics may be due, in part, to coexistent hypertension; they suggest involvement of small intramyocardial arteries in the diabetic patients, which does not occur, or occurs in a lesser degree, in the nondiabetics. An obliterative process in such vessels might then serve to impair the development of collateral circulation, and such an event would tend to increase the susceptibility to infarction and death from a second coronary occlusion. It would also tend to impair the healing of an acute infarct and, when the latter is transmural, would serve to increase the susceptibility to myocardial rupture. Vascular lesions of small arteries might also explain, at least in part, an enhanced arteriosclerotic process of cognate vessels, since they may constitute a local peripheral resistance against which the latter vessels would have to work. In the aorta, involvement of the vasa vasorum might lead to intensified plaque formation on a basis similar to syphilitic aortitis where increased intimal formation is associated with inflammatory lesions of the intramural vascular supply. The failure to observe an increased susceptibility to cerebrovascular sequelae in diabetics further suggests the importance of local phenomena dependent on the integrity of small vessels.

Three Primary Carcinomas of the Lung Arising in a Left Lower Lobe with Metastasis of 2 of the Tumors: A Case Report. W. Newman and P. C. Adkins. J. Thoracic Surg. 35:474-482 (April) 1958 [St. Louis].

The authors report on a 62-year-old man with arteriosclerotic disease of the heart, in whom thoracotomy was advised despite the patient's heart disease, since roentgenograms taken because of some pain in the left chest area revealed a pulmonary shadow which was thought to be a tumor. There was no clinical evidence of distant metastasis. Palpation of the left lung at operation disclosed 2 distinctly separate masses in the lower lobe. Large hard lymph nodes were present at the hilus and in the inferior pulmonary ligament. A left lower lobe lobectomy and hilar lymphadenectomy were performed. Examination of the surgical specimen revealed 2 primary tumors, composed of 3 histologically different variants of bronchogenic carcinoma, all arising in the lower lobe of the left lung. These variants were a well-differentiated *squamous carcinoma forming keratin "pearls,"* a well-differentiated papillary adenocarcinoma, and an undifferentiated (oat-sell) carcinoma. The latter 2 neoplasms produced metastases in regional lymph nodes of "pure strains" or "lines" of tumor with no admixture or intermingling of the oat-cell carcinoma and the adenocarcinoma in any of the metastases. There was no metastasis from the well-differentiated squamous carcinoma.

Three months after the operation the patient slipped and injured his left hip. He was readmitted to hospital, and roentgenologic examination revealed a pathological fracture of the neck of the left femur and metastatic lesions in the ribs, left scapula, and right clavicle. Internal fixation of the neck of the left femur was performed. Postoperatively the patient's condition deteriorated, and he died 4 weeks after the operation. The separate "lines" of metastasis from the left lower lobe tumor found in the hilar lymph nodes at the time of the lymphadenectomy were still evident in autopsy sections of regional nodes and distant organs. The bulk of the metastases were those of the "oat-cell" component and were found in the pancreas, kidneys, periadrenal tissues, heart, gallbladder wall, and lymph nodes. The papillary adenocarcinoma (bronchiolar component) was found in the lower lobe of the right lung, right hilar lymph nodes, and kidneys.

Because of the "pure strains" or "lines" of tumor, with no zones of transition, found in the primary sites in the lower lobe of the left lung and maintained in metastases of the regional nodes and distant organs, this case would appear to fit in the classification devised by Foulds as a rare instance of "independent primary tumors." From the clinicopathological point of view it is becoming increasingly evident that there are many interrelated and interdependent factors (rather than any single one) which are important in improving operability, survival, and salvage rate for carcinoma of the lung. Among these factors are histological type, location and size of the primary tumor, presence or absence of vascular and lymphatic invasion, and status of the margin of resection, as well as a group of only dimly envisioned "host factors." The presence of the 3 distinct primary carcinomas, with separate lines of metastasis of 2 of the tumors in this case, emphasizes the problem of multicentric against unicentric origin of carcinoma of the lung. Extensive areas of in situ carcinoma were found in the bronchus of origin adjacent to the infiltrating portion of the well-differentiated squamous carcinoma in the superior segment of the lower lobe of the left lung. Areas of in situ oat-cell carcinoma and bronchiolar adenocarcinoma were also recognized away from zones of infiltration, lending strong support to the concept of the multicentric origins of carcinoma of the lung. Among the manifold clinical implications of the concept of the multicentric origin of cancer is the paramount need for more frequent examination and closer observation of that particular organ or system of the patient in which the initial primary cancer has developed.

Accessory Lung with Persistent Left Superior Vena Cava and Duplication of Intestine. G. R. Hennigar and S. H. Choy. J. Thoracic Surg. 35:469-473 (April) 1958 [St. Louis].

The authors report a case of a true accessory lung, duplication of the intestines, and abnormal return of venous blood to the left side of the heart in a 1-month-old girl. The infant was born 1 month prematurely. From the beginning the patient had a poor appetite for an evaporated milk formula and had small, hard, and yellow stools. Because of chronic constipation, straining at defecation, and appearance of a mass at the anal orifice and of some bright red blood on the diaper, the infant was admitted to the Medical College of Virginia Hospital. A laparotomy was performed and revealed that the terminal ileum was duplicated as well as the cecum and the appendix. There was a duplicated large intestine down to and below the peritoneal reflection. The duplicated colon had a mesentery of its own from the terminal ileum up to the midtransverse colon. Surgical resection of the duplicated terminal ileum, appendix, cecum, ascending colon, and proximal transverse colon was performed. After the operation the infant did satisfactorily until the 8th postoperative day, when vomiting and subnormal temperature occurred. The respiration became difficult. There was intense cyanosis and coarse rhonchi and rales throughout the chest, and the patient died.

Autopsy revealed an aerated accessory lung lying in the posterior part of the thoracic cage and separated from the left lung by a translucent sheet of pleura. The accessory lung had communication with the trachea by an eparterial bronchus which arose from the left side of the trachea less than 1 cm. above its bifurcation. The lungs with their lobes and their contained blood supply were injected with vinylite plastic. This procedure revealed that the accessory lung was supplied on the arterial side by a branch of the left main pulmonary artery. The return of the venous blood was by the pulmonary veins. An additional anomaly was drainage of the azygos system into a left persistent superior vena cava which drained into the left atrium. It seems probable that the accessory lung should be so designated only if the following criteria are fulfilled: origin from the trachea or main-stem bronchus, a pulmonary blood supply, and a separate pleural cavity. From a review of the literature and the findings in this case, the authors conclude that the development of a true accessory lung is not brought about by the mechanism of pulmonary sequestration.

The Hydration of the Nucleus Pulposus and Its Relation to Intervertebral Disc Derangement.

N. G. C. Hendry. J. Bone & Joint Surg. 40B:132-144 (Feb.) 1958 [London].

The efficient functioning of the intervertebral disk depends largely on the elasticity of the nucleus pulposus, and this, in turn, is closely related to its water-binding capacity. In early life a water content of 80 to 88% exists. From the 4th decade onward an increasing proportion of subjects show a progressive lowering of the degree of hydration. This change is usually accompanied by an alteration in the appearance of the nucleus, which becomes amorphous and sometimes discolored and then progressively more and more fibrotic until all trace of the normal highly elastic and highly hydrated gel is lost. There is, therefore, a generally accepted concept of the process of "aging" of the normal intervertebral disk. In protruded or extruded disks, however, degeneration is observed irrespective of age. This suggests that, whether before or after displacement, deranged disks suffer either an acceleration of the normal aging process or the action of some other factor which the normal disk escapes. The author compared the water-binding capacity (and, therefore, the functional efficiency) of 18 normal disks obtained at autopsy with that of 75 mechanically deranged disks obtained at laminectomy. The normal disks were obtained from persons ranging in age from 16 to 35 years. The operation specimens were obtained from patients aged between 17 and 44 years. Commenting on the mechanism by which water is retained in the disk, the author points out that there are 2 possibilities: osmotic pressure, exerted by the individual molecules, and imbibition pressure, exerted by the protein/polysaccharide gel. The nature of imbibition pressure and its measurement are discussed.

Each specimen was weighed, first in its fresh state, then after immersion in isotonic sodium chloride solution for 24 hours, and then after desiccation over anhydrous calcium chloride under reduced pressure. A comparison of the desiccated with the fully hydrated weight showed the maximum degree of saturation of which the nucleus was capable when free from pressure; and a comparison of the desiccated with the original weight indicated the degree of saturation which the nucleus had been able to maintain under the pressure obtaining in the disk space or in the neural canal. The most convenient method of expressing these ratios, and of using them to compare one nucleus with another, is to take the desiccated weight in each case as unity and the other weights in proportion. It was found that inbibition pressure, and not osmotic pressure, is the important factor in maintaining hydration of the nucleus, and the comparison has been based on this finding. The terms "free imbibition index" and "effective imbibition index" are suggested as being readily determinable means of expressing the functional efficiency of a nucleus. A reduction in imbibition pressure was a constant feature of the specimens obtained at operation. No evidence was found to support the theory that hyperhydration or engorgement of the nucleus plays a part in disk protrusion. A reduction in imbibition pressure can, however, be expected in itself, by a combination of mechanical and hydrostatic effects, to cause disk derangements. The reduced imbibition pressure of abnormal disks is related to abnormal loss of, or deterioration in, the protein/polysaccharide of the nucleus. The premature onset of, or some disturbance in, the normal aging process is a prime cause of mechanical derangement of the disk.

Fenestration of the Semilunar Cusps and "Functional" Aortic and Pulmonic Valve Insufficiency.

B. Friedman and B. M. Hathaway. Am. J. Med. 24:549-558 (April) 1958 [New York].

The authors report on 2 57-year-old men with systemic hypertension, well-defined aortic diastolic murmur, and fenestrated aortic cusps. In the first patient, pyelonephritis and hypertension of at least 1-year duration terminated in rapidly progressing heart failure and renal failure. Auscultatory and peripheral signs of aortic insufficiency were present and contributed to the cardiac strain. The diagnosis of syphilitic aortic insufficiency figured most promgastromalacia, with extrusion of 300 ml. of acid gastric contents and remnants of food into the abdominal cavity, beneath the left leaf of the diaphragmatic dome. The 5th patient, a 24-year-old man, had sustained a severe burn from flaming oil and was admitted to hospital semicomitose and in shock. Second-degree and third-degree burns involved about 60% of the body surface. The condition of this patient deteriorated, and eventually he died in an extremely emaciated state 6 months after the accident. It should be noted that on the 18th day he had complained of epigastric pain of some days' duration, especially during the intake of milk. Four months after the accident, black vomiting occurred, and the patient became very ill with a feeble pulse. Three weeks later a similar course of events was reported. At autopsy a large ulcer, 3 cm. in diameter and at least 2 cm. deep, was present high on the major curvature. The ulcer penetrated through the diaphragm on the left side and passed into the base of the left lung, which was adherent. The 6th patient was a 52-year-old healthy man, who disappeared while skiing in the mountains and was found dead 2 days afterward. Autopsy revealed a slight cerebral edema and the presence of about 20 hemorrhagic erosions, with superficial loss of substance, scattered in the gastric mucosa. Histological examination of the gastric ulcerations revealed hemorrhagic edema with necrosis and infiltration, with a few polymorphonuclear leukocytes but neither fibrosis nor chronic inflammatory reactions. The ulcers were restricted to the mucosa.

Unilateral Pulmonary Artery Absence or Hypoplasia: Radiographic and Cardiopulmonary Studies in Five Patients. J. C. Elder, B. L. Brofman, P. M. Kohn and B. L. Charms. Circulation 17:557-566 (April) [Part 1] 1958 [New York].

This report is based on 5 patients in whom the diagnosis of unilateral absence or hypoplasia of a main branch of the pulmonary artery was suspected and eventually confirmed with the aid of special studies. As far as the authors were able to ascertain, this is the largest series in which the diagnosis was made prior to autopsy or surgical exploration. These patients showed thoracic asymmetry and disparity between the vascular markings in the lung fields. The resting pulmonary artery pressures were usually normal. On exercise there was an exaggerated rise in pulmonary artery pressures. With occlusion of a segment of the existing pulmonary vascular system by a balloon-tipped catheter, there was a marked rise in pulmonary artery pressure. There was negligible oxygen uptake on the side of the absent artery. The condition is a symptomatic clinical entity.

An Exceptional Incidence of "Accessory Spleen" in the Liver with Sclerosiderotic Gandy-Gamna Nodules. A. Cavallini. Minerva med. 49:687-690 (Feb. 24) 1958 (In Italian) [Turin, Italy].

A 36-year-old man was hospitalized for gastric ulcer. He complained of recurrent epigastric pain for the past 6 years. The onset of pain occurred 10 to 20 minutes after a meal, with disappearance shortly before the following meal. There had been a pain-free period of 1 or 2 months when this clinical disorder first appeared, which period shortened to only a few days shortly before the admission. A mild pain in the epigastric area was the only symptom established on clinical examination. Operation revealed an ulcer in the lower portion of the small curvature. A nodule, the size of a large hazelnut, was found protruding from the anterior margin of the left lobe of the liver. The resected nodule was diagnosed as splenic tissue, the presence of sclerosiderotic Gandy-Gamna nodules in it supporting this opinion. The neoplasm, classified as accessory spleen, was the result of a congenital and of an embryonic malformation of the celomic (mesothelial) epithelium. This disorder made possible the development of the accessory spleen in a deviant site.

RADIOLOGY

Changes Observed in the Intervertebral Disc After Discography. I. Goldie. Acta path. et microbial. scandinav. 42:193-197 (No. 3) 1958 (In English) [Copenhagen].

Discography is a diagnostic aid in intervertebral disk lesions. The disk is visualized roentgenologically after the injection of an opaque substance. The author made microscopic studies on 122 intervertebral disks that had been surgically removed. Fifty-three of these disks had been subjected to discography. The time that had elapsed between discography and the removal of the disk ranged from 1 week to 6 months. In 28 of the 53 disks into which contrast material had been injected, hyaline droplets were found mostly in the nucleus pulposus, but some were found also in the annulus fibrosus. The hyaline droplets were slightly stainable with periodic acid-Schiff (PAS) stain. The hyaline droplets were found in none of the 69 disks that had not been injected with contrast material, and so they are regarded as sequelae of discography. It is assumed that the hyaline droplets are the result of a reaction between the contrast medium and vital disk tissue, as they were not found in cadaver disks that had been injected with contrast medium, and as a time factor seems to be involved in their development. Moreover, no inflammatory reaction was observed accompanying the hyaline droplets.

Roentgenographic Abnormalities of the Skeletal System in Wilson's Disease (Hepatolenticular Degeneration). N. Finby and A. G. Bearn. Am. J. Roentgenol. 79:603-611 (April) 1958 [Springfield, Ill.].

Wilson's disease (hepatolenticular degeneration) is the result of an hereditary defect of metabolism which is associated with an excessive absorption of copper from the intestinal tract and consequent increased copper content of the body. Copper deposition in the brain and liver is probably responsible for the hepatolenticular degeneration. Tremor, rigidity, dysarthria, and dysphagia are a result of disorganization of the lenticular region of the brain. Cirrhosis of the liver is almost always present but is seldom the dominant clinical feature. When the disease appears in adults, it is milder and more slowly progressive than in younger patients. The Kayser-Fleischer ring, a brown or grayish green ring at the limbus of the cornea, is pathognomonic of Wilson's disease and is seen in more than 95% of the patients. Excessive quantities of copper have been found in the Kayser-Fleischer corneal ring. Similar deposits of copper in the cerebral cortex, kidney, and other tissues may be related to the mental deterioration, the renal changes, and the skeletal abnormalities occasionally seen in these patients. The authors describe the bone and joint abnormalities they had observed in 20 patients with Wilson's hepatolenticular degeneration.

Only 6 of the 20 patients in whom a roentgenographic skeletal survey was made had normal osseous structures. Seven patients showed evidence of osteomalacia; 2 of these had Milkman pseudofractures. Nine patients exhibited an unusual marginal bone fragmentation, and 11 showed roentgenologic evidence of advanced osteoarthritis despite their relative youth. The osteomalacia and Milkman pseudofractures may be related, in part, to abnormality in phosphorus metabolism. A similar association is seen in patients with the Fanconi syndrome. This syndrome is characterized by osteomalacia with multiple fractures and pseudofractures, hypophosphatemia, elevated alkaline phosphatase level, massive generalized aminoaciduria with normal plasma amino acid level and renal glycosuria. Many of these features are evident in patients with Wilson's hepatolenticular degeneration, and it has been suggested by other investigators that Wilson's hepatolenticular degeneration may be another hereditary source of the Fanconi syndrome. It is unlikely that all the skeletal abnormalities found in patients with Wilson's disease can be related to the disturbed renal function. Moreover, the bone fragmentation, osteoarthritis, and cartilage degeneration are less easily explained than the osteomalacia or pseudofractures. Thus, the possibility that the skeletal abnormality may be directly due to the abnormal copper metabolism must be considered and warrants further study. Comparative studies on the copper content of cartilage in normal subjects and in patients with Wilson's disease are now in progress.

Radiation Nephritis: A Clinicopathologic Correlation of Three Surviving Cases. S. R. Cogan and I. I. Ritter. Am. J. Med. 24:530-534 (April) 1958 [New York].

The authors studied the renal histology and clinical course of 2 women and a 14-month-old child with radiation nephritis, who survived the effects of this disease. The women were studied by means of renal needle biopsy. Nephrectomy was performed on the child when a nonfunctioning left kidney and hypertension developed after massive radiation. Pathological studies of radiation nephritis have so far been limited to tissues obtained at autopsy; they represent maximal renal damage. Luxton and Zuelzer described varying degrees of glomerular hyalinization, widespread fibrosis, tubular atrophy, and arteriolar fibrinoid degeneration. These findings were confirmed by Grossman. The findings in the authors' cases, in which biopsies were performed revealed abnormalities mainly in the glomerulus, with thickening, degenerative cellular changes, and a few areas of intertubular fibrosis. These findings represent the more moderate stages, reflecting submaximal renal damage consistent with the clinical evidence of moderate renal dysfunction and survival of the patient. These changes are the earliest seen in this disease and indicate that the glomerulus is the primarily affected portion of the kidney with secondary tubular atrophy.

An important factor which may account for the apparent rarity of this syndrome is lack of awareness of its existence by the clinician and the roentgenologist. Follow-up studies of the renal status in patients receiving abdominal radiation appear not to be made. Furthermore, the relationship of the renal disease to the abdominal radiation may not be suspected and is uncovered only by chance. The authors believe that it is important to establish the true incidence of this hazard of radiation therapy in order that steps may be taken to prevent its occurrence.

So-Called "Meigs' Syndrome" Associated with Benign and Malignant Ovarian Tumors. J. F. Mokrohisky. Radiology 70:578-581 (April) 1958 [Syracuse, N. Y.].

The author reports on a 59-year-old woman with a fibroma of the left ovary and a 52-year-old woman with bilateral cystoadenocarcinoma of the ovaries, in whom the tumor was associated with ascites and hydrothorax. Repeat roentgenograms, taken 5 and

9 months, respectively, after removal of the tumor, showed that the effusions had disappeared. Meigs's syndrome is a relatively uncommon occurrence. It may occur with fibroma of the ovary. It has also been reported with other benign ovarian tumors and occasionally with a malignant ovarian tumor. Ascites and hydrothorax associated with a malignant ovarian tumor do not indicate secondary metastatic implants of the peritoneum and pleura, since such implants were not observed at the time of surgical removal of the tumor in the patient with cystoadenocarcinoma. Nine months later this patient was readmitted to hospital because of recurrent ovarian tumor involving the rectum, sigmoid, and terminal ileum. An enteroenterostomy and a sigmoid colostomy were performed. The chest and abdomen continued to be free of fluid. In this patient, the effusion disappeared permanently after removal of the malignant tumor, as it did in the first patient after removal of the benign tumor. It thus becomes important to recognize the benefits of surgical removal of the tumor, whether benign or malignant, and not to regard the patient's condition as hopeless.

PHYSIOLOGY

Serotonin, Norepinephrine, and Related Compounds in Bananas. T. P. Waalkes, A. Sjoersma, C. R. Creveling and others. Science 127:648-650 (March 21) 1958 [Washington, D. C.].

Waalkes and associates began chemical studies to explain Anderson's observations that ingestion of bananas produces an increased urinary excretion of the serotonin (5-hydroxytryptamine) metabolite, 5-hydroxyindoleacetic acid. The studies revealed that bananas contain large amounts of 2 physiologically important agents, serotonin and arterenol. The presence of these potent physiological agents in a food as widely used as the banana is of clinical interest. Serotonin is known to inhibit gastric secretion and to stimulate smooth muscle in the intestine and elsewhere; arterenol is an important mediator of autonomic function and is used extensively as a vasoconstrictor agent. Whether the oral administration of these amines through banana feeding can have effects on the gastrointestinal tract or on the cardiovascular system remains to be determined. It is of immediate clinical significance that ingestion of bananas may lead to erroneous chemical diagnoses of carcinoid tumors and pheochromocytoma by producing an increased urinary excretion of serotonin and arterenol and their metabolites. Also, bananas should be eliminated from the diets of patients whose urinary indoles and catecholamines are being measured for other purposes; for example, in mental disease. It remains to be determined whether other edible plants contain these agents.

Diet, Physical Activity and the Serum Cholesterol Concentration. H. L. Taylor. Minnesota Med. 41:149-153 (March) 1958 [St. Paul].

A number of factors influence the level of serum cholesterol, the most important being diet and sex hormones. Exercise with its demands for calories influences the diet. Of the several dietary parameters which might affect cholesterol metabolism in man, the caloric balance, the quantity of dietary fat, and the type of fat consumed have been shown to be important factors affecting the serum cholesterol concentration. The caloric balance can have marked effects on this concentration. A negative caloric balance will produce a fall in the serum cholesterol concentration, while a positive caloric balance will produce an increase. The author cites earlier experiments on the acute effects of exercise and tabulates and explains the results of 3 experiments on the effect of increasing the daily physical activity on the serum cholesterol concentration. He believes that the lipoprotein cholesterol complex can be regarded as a vehicle for the transport of fat from one important metabolic site to another. Current concepts regarding the mechanism of fat transport are emphasizing 2 general pathways for transport. One concept focuses on the lipoproteins, the other on nonesterified fatty acids, but these are not viewed as mutually exclusive.

There is evidence that the fats are extensively hydrolyzed in, or in close proximity to, the intestinal wall and are then reassembled as neutral fat and are transported as such in the chylomicrons that characterize the lipemic phase. There is little doubt that much of the absorbed fat is temporarily deposited as such in the liver. It is with the subsequent events, the transport of fat from the liver to the tissues and the mobilization of fat from depots elsewhere, that the author is mainly concerned. There is evidence that under some conditions fat transport in the lipoproteins is important. For example, infants suffering from the general protein deficiency represented in kwashiorkor have grossly enlarged livers loaded with fat and low levels of serum cholesterol from which we infer similarly low levels of lipoproteins in the blood. When such infants are treated simply by feeding proteins or even a mixture of amino acids, the liver rapidly loses its fat, the subcutaneous fat depots are repleted, and in the process the level of serum cholesterol rises. On the other hand, large movements of fat from the depots to working muscles occur with no corresponding rise in cholesterol or lipoprotein concentration in the blood, and there may even be a fall.

The hypothesis that the lipoproteins play an important role in the transport of fat from liver to fat depot or tissues appears to be consistent with some observations that are listed. The findings presented appear to be consistent with the hypothesis that the lipoprotein cholesterol transport system can be largely bypassed during exercise. In the experiments under consideration, the exercise took place in a comparatively short time. If one is to judge by the slow increase in the serum cholesterol concentration after imposing a heavy fat load without changing the caloric requirement, fat transport by the lipoprotein cholesterol system is a slow but probably continuous process. The circulation between liver and skin or other fat depots is probably not much influenced by such a short intensive bout of exercise. It is suggested that the relation of exercise to meals may be important and that exercise at a lower rate, spread over a longer period of time, may have somewhat different effects. A number of questions have yet to be answered regarding the effects of exercise on the serum cholesterol concentration. Nevertheless, it can be stated that physical activity can allow man to increase the total quantity of fat ingested without a parallel increase in the serum cholesterol concentration and that exercise can alter the response of the serum cholesterol to dietary manipulation.

PUBLIC HEALTH

Chemoprophylaxis with Isoniazid in Antituberculosis Dispensaries. F. Luccioli and E. Marino. Lotta contro tuberc. 27:1177-1179 (Dec.) 1957 (In Italian) [Rome].

Zorini introduced in Italy chemoprophylaxis with isoniazid for control of tuberculosis in infants and children. The authors applied Zorini's chemoprophylactic scheme in 100 children, aged between 6 and 12 years, who live in a community antituberculous dispensary. The children came from homes where tuberculous infection had been present. Some children presented positive and some negative reaction to the cutaneous tests. Manifest renal and liver functional disorders were corrected in the affected children before instituting chemoprophylaxis. Intracutaneous and cutaneous tuberculin tests were made at the onset and at the termination of each course of administration of isoniazid. The drug was given in the form of sirup or tablets in daily doses of 20 mg. per kilogram of body weight to children who had a positive reaction to the cutaneous test and of 10 mg. per kilogram of body weight to those who were negative to the cutaneous test. This prophylactic scheme consisted of 2 courses of treatment, each of a duration of 3 months, with a drug-free period of 9 months in between. Isoniazid was well tolerated by the children, and its toxicity was negligible. The treatment has not yet been completed. The following objective findings have been observed until now: general gain in body weight; stabilization of the reaction to the tuberculin test in 55 children; decrease of the reaction in 30; and reversal of the reaction in 15. The authors plan to apply this chemoprophylaxis with isoniazid for control of tuberculosis on a broad community basis after the study on this series of children has been completed.

Poisonous Fi[illegible] B. W. Halstead. Pub. Health Rep. 73:[illegible] 1958 [Washington, D. C.].

The public health significance of poisonous fishes was pointed up in the series of outbreaks which occurred in Midway, Johnston, and the Line Islands, beginning about 1943 and reaching a peak about 1946. Recent mass intoxications in the western Pacific have once again directed attention to poisonous marine organisms. These outbreaks began about 1952, became increasingly severe during 1955, and have continued until the present time, resulting in the intoxication of more than 40,000 persons. Most of the outbreaks have taken place in Japan, the Philippine Islands, and more recently Vietnam. The causative agents were as follows: octopus, Octopus vulgaris, O. döfleini; squid, Omnastrephes sloani pacificus; Japanese horse mackerel, Trachurus japonicus; common Japanese mackerel, Scomber japonicus; flying fish, Prognichthys agoo; and oceanic bonito, Katsuwonus pelamis. All the outbreaks have been seasonal, taken place from June to the middle of September. Bacteriological tests have been negative, and the degree of freshness of the organisms seems to have no bearing on the matter. The symptoms are similar to those produced by bacterial food poisoning, but no human pathogens have been isolated by Japanese epidemiologists. The mortality rate in the largest outbreaks in 1955 was 0.77%.

Fishes are believed to become poisonous as a result of their food habits—feeding on marine algae. There is no evidence that plankton or radioactive substances are a factor in the production of the poisons. Poisonous fishes are largely circumtropical in their distribution. Toxin content is greatest in puffers during their reproductive season of the year, but this is probably not true of most other fishes. The distribution of the toxin within the body of the fish is subject to considerable fluctuation, but if the fish is poisonous, some of the poison will be present in the viscera in about 90% of the cases. Poisonous fishes cannot be detected by their appearance. Fish poisoning should not be confused with bacterial food poisoning, with which it has no etiological connections. The over-all incidence of fish poisoning is not known. Eight clinical types of ichthyosarcotoxism are recognized at present. With the exceptions of gempylid diarrhea and scombroid poisoning, all other types of ichthyosarcotoxism are characterized by neurotoxic symptoms. The treatment of fish poisoning is symptomatic.

9 months, respectively, after removal of the tumor, showed that the effusions had disappeared. Meigs's syndrome is a relatively uncommon occurrence. It may occur with fibroma of the ovary. It has also been reported with other benign ovarian tumors and occasionally with a malignant ovarian tumor. Ascites and hydrothorax associated with a malignant ovarian tumor do not indicate secondary metastatic implants of the peritoneum and pleura, since such implants were not observed at the time of surgical removal of the tumor in the patient with cystoadenocarcinoma. Nine months later this patient was readmitted to hospital because of recurrent ovarian tumor involving the rectum, sigmoid, and terminal ileum. An enteroenterostomy and a sigmoid colostomy were performed. The chest and abdomen continued to be free of fluid. In this patient, the effusion disappeared permanently after removal of the malignant tumor, as it did in the first patient after removal of the benign tumor. It thus becomes important to recognize the benefits of surgical removal of the tumor, whether benign or malignant, and not to regard the patient's condition as hopeless.

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Diet, Physical Activity and the Serum Cholesterol Concentration. H. L. Taylor. Minnesota Med. 41:149-153 (March) 1958 [St. Paul].

A number of factors influence the level of serum cholesterol, the most important being diet and sex hormones. Exercise with its demands for calories influences the diet. Of the several dietary parameters which might affect cholesterol metabolism in man, the caloric balance, the quantity of dietary fat, and the type of fat consumed have been shown to be important factors affecting the serum cholesterol concentration. The caloric balance can have marked effects on this concentration. A negative caloric balance will produce a fall in the serum cholesterol concentration, while a positive caloric balance will produce an increase. The author cites earlier experiments on the acute effects of exercise and tabulates and explains the results of 3 experiments on the effect of increasing the daily physical activity on the serum cholesterol concentration. He believes that the lipoprotein cholesterol complex can be regarded as a vehicle for the transport of fat from one important metabolic site to another. Current concepts regarding the mechanism of fat transport are emphasizing 2 general pathways for transport. One concept focuses on the lipoproteins, the other on nonesterified fatty acids, but these are not viewed as mutually exclusive.

There is evidence that the fats are extensively hydrolyzed in, or in close proximity to, the intestinal wall and are then reassembled as neutral fat and are transported as such in the chylomicrons that characterize the lipemic phase. There is little doubt that much of the absorbed fat is temporarily deposited as such in the liver. It is with the subsequent events, the transport of fat from the liver to the tissues and the mobilization of fat from depots elsewhere, that the author is mainly concerned. There is evidence that under some conditions fat transport in the lipoproteins is important. For example, infants suffering from the general protein deficiency represented in kwashiorkor have grossly enlarged livers loaded with fat and low levels of serum cholesterol from which we infer similarly low levels of lipoproteins in the blood. When such infants are treated simply by feeding proteins or even a mixture of amino acids, the liver rapidly loses its fat, the subcutaneous fat depots are repleted, and in the process the level of serum cholesterol rises. On the other hand, large movements of fat from the depots to working muscles occur with no corresponding rise in cholesterol or lipoprotein concentration in the blood, and there may even be a fall.

The hypothesis that the lipoproteins play an important role in the transport of fat from liver to fat depot or tissues appears to be consistent with

QUESTIONS AND ANSWERS

HEREDITARY HEARING LOSS

To the Editor:—*A 53-year-old man, otherwise healthy, has had a slowly progressing high-tone deafness ever since the age of 18, when he took 10 grains (0.65 Gm.) of quinine sulfate daily for two weeks as a malarial prophylaxis. Recent audiometric tests revealed 42% hearing loss in one ear and 48% in the other. This is a steep drop, from about a 20-db. loss at 2,000 cps to a 60-db. loss or more in the higher frequencies. Hearing loss and tinnitus are definitely worse in cold, damp weather and after upper respiratory infections. How can the present residual hearing be conserved? Specifically, is a change of climate from western Washington to a high, dry, sunny area worth considering? What is the likelihood of further auditory nerve damage from tobacco, alcohol, barbiturates, salicylates, exposure to x-rays, or exposure to ultrasonic radiation? Is any specific treatment other than nicotinic acid worth considering?*

M D., Washington.

Answer —The opinion of this consultant is that the patient has a hereditary type of nerve impairment Unfortunately, there is no medical or surgical treatment that will improve or necessarily maintain his present residual hearing. A change of climate would not be of any permanent benefit, and the stimulants and exposures mentioned would not further contribute to the hearing loss as long as moderation was observed. There is no specific treatment for this condition other than aural rehabilitation, such as lip reading and auditory training. The latter would include the use of a hearing aid if necessary. Fortunately, this type of patient will always be able to hear, at least by means of a hearing aid.

TOXIC DOSE OF ANTIBIOTICS

To the Editor:—*What is the toxic or lethal dose of any of the antibiotics (i. e., not the sensitizing dose or that which allows intestinal overgrowth)? Can an infection be cured by one very large dose of an antibiotic?*

Jacob Greenblatt, M.D., Stamford, Conn.

Answer —To the best of this consultant's knowledge, the lethal doses for man of the various antibiotics have never been determined. Furthermore, there is a great variation in the doses of the approximately 19 antibiotics now available to the general practitioner that will produce toxic reactions in man. For example, 100 million units of penicillin may be administered daily without difficulty, while nephrotoxicity has been noted with bacitracin after 10 daily doses of 40,000 to 80.000 units have been given intramuscularly. The "Handbook of Toxicology, vol. 2, Antibiotics," edited by Spector (Philadelphia, W. B. Saunders Company, 1957) has been prepared with considerable care under the direction of the Committee on the Handbook of Biological Data, Division of Biology and Agriculture, the National Research Council, and gives a general picture of those doses which have proved clinically to produce toxic reactions in man. Several infections are cured by single doses of antibiotics. For example, gonorrhea is cured in over 90% of the cases with a single injection of 300,000 units of penicillin. Similarly, primary and secondary syphilis is cured in 90% or more of the cases with a single injection of 2,400.000 units of long-acting penicillin. Furthermore, such infections as Vincent's angina and mild sore throat caused by streptococcic infection are also cured, in the majority of cases, by a single dose of penicillin, 600,000 to 1 million units given intramuscularly, particularly when the prolonged acting penicillin salts are utilized.

CHEMICAL PREVENTION OF CORONARY NECROSIS

To the Editor:—*Dr. Hans Selye is reported to have prevented coronary infarction in rats by administering magnesium and potassium before exposure to stress. Is there a magnesium preparation which is absorbable with oral use?*

Robert S. Srigley, M.D., Altus, Okla.

Answer.—It is not yet definitely established whether the massive myocardial necroses produced by Selye in animals (by exposure to stress after humoral conditioning) are essentially identical with coronary infarct in man. For a discussion of the similarities and differences between the experimental and clinical lesions, see Selye, The Chemical Prevention of Cardiac Necrosis (Chicago, the Ronald Press Company, 1958; *Brit. M. J.* 1:599, 1958). However, in these experiments, orally given magnesium chloride was sufficiently well absorbed to prevent the cardiac necroses. Magnesium sulfate was virtually ineffective.

The answers here published have been prepared by competent authorities They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

SERORESISTANT SYPHILIS

To the Editor:—*A 42-year-old man, admitted to the hospital on June 1, 1957, because of a bleeding duodenal ulcer, showed positive reactions to Kahn and Venereal Disease Research Laboratory (VDRL) tests. These results were verified by both the county and a private clinical laboratory. Kolmer's test was reactive (44444440) at 64 dilutions. He was given 600,000 units of sterile benzathine penicillin G suspension intramuscularly for 10 successive days. In July, 1957, the colloidal gold test of the spinal fluid showed a reaction of 1233210000, with chlorides, 705 mg. per 100 cc., and the finding in Kolmer's test was negative. In August, the blood again showed positive reactions to VDRL and Kolmer's tests (the latter at 32 dilutions). Penicillin injections were given again, this time 1 million units triweekly for six doses. On Feb. 18, 1958, the finding in the VDRL test was 3+ and in the Kolmer test 444320 at 32 dilutions. This patient had no evidence of syphilis on physical examination, and he denied a history of primary or secondary signs or symptoms. Another patient, 58 years old, was hospitalized for an acute respiratory infection in August, 1957. His blood showed a 2+ reaction in the Kahn test. He was given two courses of therapy similar to those of the first patient. On Feb. 25, 1958, he showed a positive reaction in the Kolmer test (44420) at 8 dilutions and a weakly positive reaction to the VDRL test. Findings in the Wassermann test of spinal fluid were negative on Oct. 2, 1957. Please give advice on further treatment for these two patients.*

M.D., California.

Answer.—Both of these patients have already received adequate treatment for syphilis. They are seroresistant, a phenomenon which is usual when treatment is given for syphilis after the early stages of the disease. The strongly positive serologic tests in the first case leave little doubt of the diagnosis. The second patient probably has syphilis also, because of the persistence of positive findings in serologic tests for six months after the acute respiratory infection, but there remains a possibility that these are "biologic false-positive" results. It might be worthwhile in this instance to do one of the more specific tests with the treponemal antigens (Treponema pallidum immobilization test, Treponema pallidum complement-fixation test, Treponema pallidum immune adherence test, or Reiter complement-fixation test). Epidemiologic investigation is not mentioned by the correspondent but should certainly be done if it has not been already. Periodic reexamination of each patient is indicated, but further therapy should not be given on a basis of a positive serologic test alone.

COMMON LAVATORY FACILITIES FOR YOUNG CHILDREN

To the Editor:—*The following question has come up for debate between several parents and educators in this area: Should nursery school children be encouraged to use the same lavatory facilities with both boys and girls present at the same time? If so, at what age may this be begun, and at what age should separate "boys' room" and "girls' room" use be initiated? If not, what are some possible arguments against this radical departure from old-fashioned modesty?*

Leonard Casser, M.D., Cresskill, N. J.

Answer.—Use of the same toilet facilities by boys and girls of nursery school age is a common practice and, in general, should be encouraged. For children who may not have brothers or sisters, it creates the natural conditions of a family atmosphere, where children normally observe each other early in life and learn to know and accept the fact of physical differences between boys and girls. It robs these differences of mystery, satisfies the normal childhood curiosity about bodily structure, and permits the expression of any anxiety or confusion that may be inherent in the situation for some children. This common exposure through use of joint toilet facilities is appropriate through the age of 4 years. At about the age of 5, when the children are in kindergarten, a conservative view would dictate the provision of separate facilities. There are no principal arguments against this practice, but there may be some practical ones. The parents of the child should themselves be in agreement with the school that the practice is acceptable; otherwise, there may easily be for the child some confusion as to discrepancies in the attitudes of adults, as represented by the teacher on the one hand and parents on the other. Parents should understand and be able to support the principles and practices represented and utilized by the schools their children attend.

PHOTOGRAPHING THE NEWBORN INFANT

To the Editor:—*It has recently become a routine practice in the local hospital nursery for photographs to be taken of newborn infants. The babies are photographed within the first three to four days of life, and a flash bulb is used. Could this cause injury to the eyes of the newborn infant?*

Sidney W. Berezin, M.D., Spring Valley, N. Y.

Answer.—There is no evidence that photographs taken during the first few days of life injure the infant's eyes. When retrolental fibroplasia was first noticed among premature babies, this question was studied rather carefully in some hospitals and it was concluded that no harm was done.

MULTIPLE EYE DISEASES

To the Editor:—*A patient with failing vision has hypertensive cardiovascular disease; her systolic blood pressure frequently is much above 200 mm. Hg, when she stops taking medicine to reduce it. Her eyes show definite evidences of changes due to hypertension and arteriosclerosis and she also has retinitis pigmentosa. There is some atrophy of the optic papillae and some degeneration of the retina. One eye specialist made a diagnosis of retinitis pigmentosa also and of asteroid hyalitis. This refers to the many flakes of material that float about in the vitreous humor of both her eyes. What medicine or treatment would help this woman's eyes and vision?*

M.D., Wisconsin.

Answer.—This patient apparently has multiple eye problems. One at a time, they are as follows: 1. Retinitis pigmentosa is a congenital, degenerative disease of the retina resulting in constriction of the peripheral visual field and, generally, in small, posterior, polar cataracts. A family history of intermarriage will probably be found. Treatment is discouraging, but some hope has been evinced by recent reports in the European literature. Doctors there use injections of placental extract or autoblood (5 cc. of the patient's own blood injected into the buttocks weekly) and report good results. 2. Hypertensive retinitis produces hemorrhages, exudates, and reduced circulation in the retina. This inevitably leads to loss of visual field and damage to the macula. The treatment is that of the underlying condition. Large doses of vitamin C and the bioflavonoids are sometimes helpful. Shortwave diathermy might also be useful. 3. Asteroid hyalitis is a degeneration of the vitreous with soapy deposits, producing the characteristic "snow storm" in the media. Generally, it does not affect vision adversely. There is no treatment for this condition.

HUSBAND AS BLOOD DONOR FOR WIFE

To the Editor:—*What are the contraindications, if any, to transfusion of a woman with her husband's blood? Would the wife be sensitized so that conditions simulating Rh factor conflict and erythroblastosis fetalis might occur in following pregnancies?*

Edmund J. Morgan Jr., M.D.
Pago Pago
American Samoa.

Answer.—At the present time, more than 30 different blood factors have been identified, belonging to at least 10 independent blood group systems. Obviously, it would not be practicable when selecting a donor for blood transfusion to insist on complete agreement between patient and donor with respect to all these blood factors. Luckily, aside from A, B, and Rh_0, the blood factors are only weakly antigenic, so that deliberate injections of blood containing a factor absent from the recipient's blood rarely gives rise to isosensitization. Therefore, blood banks find it sufficient to classify blood according to the four A-B-O groups and the Rh_0 factor (eight types in all) and to rely on cross matching tests to detect incompatibilities with respect to other blood factors. Theoretically, it might be considered objectionable to transfuse the husband's blood into a woman, since, if his blood contains a blood factor lacking from her blood, this might sensitize her, so that a baby subsequently born having this blood factor might have erythroblastosis. This danger is real in the case of Rh_0 sensitization, but, so far, there have been no reports of cases of erythroblastosis caused by sensitization to factors other than Rh_0 traceable to this source. Thus, the danger seems quite remote in view of the low antigenicity of the blood factors other than A, B, and Rh_0. A Kell-negative woman married to a Kell-negative man is much safer receiving blood from her husband than from random donors, some of whom might be Kell positive and who might thus cause sensitization and a serious hemolytic reaction. This is well illustrated by the near fatal hemolytic transfusion reaction due to Kell sensitization reported by Wiener and co-workers (*J. Lab. & Clin. Med.* 42:570, 1953). In this case, unfortunately, the Kell-negative husband could not be used as donor because his blood group was A and the patient's was O. Evidently, no blanket rule regarding the use of husbands as donors for blood transfusion would be wise, and each case should be individualized according to the circumstances.

PASTEURIZATION

To the Editor:—*Pasteurization of milk originated at a time when there was little or no examination of cows. Please list all the known natural substances and immunobiological factors that are destroyed or in any way affected through the various processes of pasteurization.*

C. D. J. Generales, M.D., Ph.D., New York.

Answer.—Pasteurization does not affect any important food substances, immunobiological factors, or enzymes that are obtained from milk except thiamine and ascorbic acid. When milk is used as the main food, as in infant feeding, it should be supplemented with ascorbic acid. As to the history of pasteurization, it was first introduced into the United States in the 1890's and gradually was accepted in some of the larger cities. During this period veterinary medical examination of cows for tuberculosis and mastitis was required in many communities. After World War I, pasteurization requirements were adopted by many health departments across the country. During the past 10 years, pasteurization has become compulsory in some states and nearly all urban areas. More than 90% of the marketed milk consumed in the United States today is pasteurized.

PERIPHERAL NERVE DEGENERATION AND VITAMIN B_{12}

To the Editor:—*In Hungary, vitamin B_{12} has become a stand-by, administered rather indiscriminately by general practitioners to almost all patients suffering from diseases of the locomotor system. While it is a correct prescription in cases of funicular myeloses consequent to pernicious anemia, is there any point in giving the drug to patients with neuritis of a widely different etiology, such as sciatica, brachialgia, and secondary affections due to cervical compression? If this therapy is justified, what would be its pharmacological workings?*

A. de Chatel, M.D., Budapest, Hungary.

Answer.—There is no evidence that vitamin B_{12} has any effect whatever on the rate of regeneration or on the prevention of degeneration in peripheral nerves.

AUTOPSY AND EMBALMING

To the Editor:—*The consultant's answer to the query concerning the performance of autopsies on embalmed bodies in* The Journal, *April 19, 1958, page 2100, is at variance with my experience. The small effort required to familiarize oneself with the appearance of arterially embalmed tissues is more than amply compensated for by scheduling for convenience and the cooperative attitude of appreciative funeral directors. In this community the funeral directors secure many autopsy permits, some even after the attending physician has been unsuccessful. Attention is invited to the comments of Parsons and of Kernohan (Letters to the Editor;* Am. J. Clin. Path. 26:*305, 306, 1956) regarding this practice.*

D. R. Dickson, M.D.
320 W. Pueblo St.
Santa Barbara, Calif.

To the Editor:—*The recent answer to the question on autopsy and embalming appears to be quite misleading because of the omission of many pertinent considerations. It is true that color and texture are somewhat changed, but a competent pathologist soon learns to appreciate and evaluate these differences. On the other hand, the hardening process produces superb brain fixation, and the brain may be sectioned immediately as thin as one likes with excellent results. The microscopic picture is unaltered in all organs. As far as emboli or thrombi are concerned, it must be remembered that the arterial injection is accomplished in the direction of blood flow under relatively low pressures. Emboli, instead of being swept away, will usually be more tightly engaged by this process. Perhaps the most serious omission in the answer is in the area of amount of embalming to be permitted before autopsy. This should be limited to arterial injection and venous drainage. Absolutely no cavity is allowable. This arrangement is readily acceptable to the funeral directors, since it serves their purpose, i.e., ease of injection through one site. Furthermore, no foreign material is introduced into the body cavities to confuse the picture. Preautopsy injection allows the pathologist to forget about ligating vessels, which becomes a tedious procedure when removing the neck organs and tongue. On completion of the examination, cavity powder, instead of liquid, may be added to preserve and harden the viscera prior to restitution of the body, almost guaranteeing a leak-proof closure. The question about safety and infection was not answered. Embalming does not completely sterilize the body. Formaldehyde is a slowly penetrating agent and a relatively poor disinfectant. It has been demonstrated many times that tubercle bacilli are often culturable after prolonged formaldehyde fixation. To disregard the fundamental safety precautions about infection because the body has been embalmed is most unwise. Embalming will render toxicological analysis impossible (with few exceptions, such as heavy metals) and will interfere to a greater or less degree with the bacteriological studies. However, most of the cases necessitating these procedures can be determined beforehand by close liaison between attending physician and pathologist, and these bodies can always be examined immediately.*

G. W. Thoma, M.D.
715 Market St.
Galveston, Texas

The above comments were referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Adaptations or deviations from standard procedures are made to suit local circumstances or to circumvent a resistance. The writers of both letters emphasized this feature and apparently recognize the disadvantages of embalming fluids in autopsy examinations. Good fixation of the brain is realized also, with flotation in proper fixative solutions.*

WASHINGTON NEWS

FROM THE WASHINGTON OFFICE OF THE AMERICAN MEDICAL ASSOCIATION

Dr. Larson Says He Will Concentrate on Better Care for Aged . .
House Committee Holds Hearings on VA's Hospital Program . .
Services Consider Doubling Civilian Medicare Charges . .

DR. LARSON WILL CONCENTRATE ON HEALTH PROBLEMS OF THE AGED

Dr. Leonard Larson, recently elected chairman of the American Medical Association's Board of Trustees, has promised to concentrate his attention on problems of the medical care of the country's aged. Dr. Larson so told the House Ways and Means Committee, where he appeared as an A. M. A. witness to oppose the Forand bill for hospitalization under social security. Also testifying was Dr. Frank Krusen of the Mayo clinic. Dr. Larson described his interest in this problem in reply to questions from Rep. Aime J. Forand (D., R. I.), sponsor of the hospitalization bill.

Mr. Forand had challenged the motives behind the Joint Council for the Health Care of the Aged, formed by the A. M. A., American Hospital Association, American Dental Association and American Association of Nursing Homes.

Dr. Krusen explained the council had been established in April but that it had been planned long before that and was "developing an aggressive program" to solve the problems of the aged.

"We are devoted to caring for the sick," he told Mr. Forand, "and we oppose this bill because it is not the right way." Earlier he described the leadership that the A. M. A. has for years supplied in efforts against chronic illnesses.

When Mr. Forand complained that the A. M. A. was "blindly opposing" his bill, yet had "nothing definite or concrete" of its own to offer, Dr. Larson replied:

"As chairman of the Board of Trustees I shall devote all my energies to solving this problem and other problems of medical care plans in general. This is my primary interest. I rise or fall on what happens in this field."

With 11 days of hearings completed on the Forand bill and other phases of social security, the committee now will decide in executive session which amendments to recommend. Indications are that there will not be an omnibus bill but that possibly there will be (a) an increase in both OASI and public assistance payments and (b) an increase in the amount of taxable income from $4,200 to $4,800 to pay for the extra benefits.

Among the last witnesses were representatives of the American Hospital Association and the American Dental Association.

For the AHA, Ray Amberg, president-elect of the Association, and Dr. James P. Dixon, chairman of its committee to study health needs of the aged, went into detail on the financial problems in providing hospital and medical care for the aged. They said the AHA had concluded that voluntary health insurance could not do the job without some form of federal help. While admitting that the social security approach might have to be resorted to ultimately, they declared that the AHA was not supporting the Forand bill "at this time."

Dr. Dixon explained that the AHA was proposing that an advisory committee (with leaders from business, labor, and the academic world, as well as from health fields) be appointed and instructed to report back to the Ways and Means Committee before Jan. 1, 1960.

"I should hope," Dr. Dixon said, "that among the assignments of such a group would be a careful appraisal of the ways in which the government might participate, and of the dangers which we think are inherent in governmental financing of hospital care of the aged, and an examination of ways in which, under an OASI or any other approach, those dangers might be avoided or minimized. . . . We believe that some such plan holds the best hope of moving fairly quickly toward a consensus on the difficult and complex issues involved, and thus toward action to meet the pressing problem that we know exists."

Drs. Matthew Besdine, a member of the ADA's council on legislation, and R. H. Friedrich, secretary of the association's council on dental health, testified for the dentists. Said Dr. Besdine:

"With due regard for and in full recognition of the fact that deficiencies may exist in the availability of health care for some of our older citizens, the association is convinced that (the Forand bill) does not provide a practical or desirable solution to the problem; the association is equally convinced that there are other more efficient, more economical programs which can and should be expanded to meet the problem."

Dr. Friedrich further explained the ADA's reasoning:

"The association recognizes that there may be a serious health problem involving many of this country's older people. The association does not, however, agree with the assumption that the number of aged persons unable to meet the costs of their health care needs approximates the number who would be entitled to receive hospital and surgical care under the provisions of H. R. 9467.

"Nor does the association agree that the primary need of all aged persons is for the kinds of health care specified in the bill. There is need for intensive research in ascertaining the number of aged people in need of health care assistance, in identifying their needs, and in devising the methods best suited to meet these needs. In this connection, there

(Continued on next page)

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Lown, B., and Levine, S. A.:
Current Concepts in Digitalis Therapy, Boston,
Little, Brown & Company, 1954, p. 23, par. 2.

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is much evidence that many of the problems of the aged stem from environmental and social factors rather than physical health factors."

Without mentioning the Forand bill as such, the American Nurses Association supported the idea of using the social security system for medical care of the aged. Julia C. Thompson, R.N., assistant executive secretary of A. M. A., testified that the dimensions of the problem of health care for older people are such "as to require the extension of the most universally held insurance—old age, survivors and disability insurance—to include health protection for its beneficiaries." Such insurance, when paid for during the working years, would be less costly to the community than tax-supported public relief, the witness argued.

The Physicians Forum also supported the Forand bill, urged social security coverage for physicians, and devoted much of its testimony to criticism of the A. M. A. One of the forum's spokesmen, Dr. Allan M. Butler of Harvard, declared:

"The Physicians Forum enthusiastically endorses the medical care section of Rep. Aime Forand's 'Social Security Amendments of 1958.' This bil would correct, to a significant degree, one of th major deficiencies of American health insurance-inadequate coverage of the aged. What is mor important, it does this in a way which meets mos of the Physicians Forum's long-standing criteria fo satisfactory health insurance plans."

Among many groups opposing the Forand bi were the International Association of Accident an Health Underwriters and the Commerce and Industry Association of New York.

HOUSE HEARINGS OPEN ON VETERAN HOSPITALIZATION

The House Veterans Affairs Committee is launching a new series of hearings on the Veterans Administration's hospital program. From them ma come legislation spelling out clearly just who entitled to care in VA hospitals and perhaps to s a ceiling an beds.

The issue, a perennial one, arose when Chairman Teague of the Veterans committee asked the administration for an explanation of why some 5,000 beds were being shut down through action of the Budget Bureau. In subsequent correspondence, the VA made public a study showing that the number of veteran patients with service-connected disabilities will decline steadily over the next 29 years, falling from 39,000 in 1957 to 23,600 in 1986.

During the same period, largely because of the increase in the number of older veterans, non-service-connected cases in both federal and nonfederal hospitals will rise from about 150,000 to 300,000, according to the VA projections. VA administrator Sumner Whittier commented: "In the light of these estimates, it is clear that there is a need for discussion and resolution of questions as to the policies for veterans' hospitalization in the future."

The American Medical Association has long advocated a clear-cut policy statement from Congress on just who is and is not entitled to VA medical care. The A. M. A. feels that as a long-range policy the provision of medical care for veterans with non-service-connected disabilities by the federal government is unsound and that the final consideration of their care must be ultimately predicated on a concern for the health and welfare of the entire population, not just a particular segment. With the existing authority on eligibility for hospital and domiciliary care subject to differing interpretations and frequent clashes between Congress and the executive agencies, the time may be at hand for new legislation.

SERVICES CONSIDER DOUBLING CHARGES FOR CIVILIAN MEDICARE

In testimony before the defense subcommittee of the Senate Appropriations Committee, Navy Surgeon General B. W. Hogan said the services were considering increasing from the first $25 to the first $50 the charge against dependents who use civilian facilities in the Medicare program.

Admiral Hogan explained that it would be several weeks at least before a directive covering this and other changes can be sent out.

He also said two other contemplated restrictions would require dependents residing on posts or in Capehart or Wherry housing (U. S. subsidized and generally near posts) to use military medical facilities exclusively and would limit the amount of elective surgery for dependents.

At the same time Admiral Hogan asked the subcommittee to restore $2,100,000 cut by the House from the Navy's Medicare funds and to delete a House amendment that would prevent the services from spending more than 60 million dollars on the civilian phase of Medicare. He said the funds would have to be restored if the Navy is to provide dependents with the medical care authorized by Congress when it enacted the Medicare program.

Military witnesses have told the subcommittee that if these restrictions aren't lifted, the civilian part of Medicare will have to be scrapped and a new and far more restrictive program worked out. House sponsors of the restrictions have virtually agreed to accept any reasonable compromise worked out in the Senate.

Admiral Hogan also said that Medicare had brought about a 29% reduction in the number of deliveries at military facilities. He declared that a study showed the cost per patient day for dependents in civilian facilities was $50.85 in contrast to $16.24 in Navy facilities, the latter figure including not only the support provided by the budget but the pay and allowances for all military personnel as well, including doctors, nurses, and corpsmen.

These and similar military figures have been challenged repeatedly in nonmilitary studies of the comparative costs.

MISCELLANY

The Atomic Energy Commission will provide $36,269 in nuclear materials for a reactor under construction at the University of Virginia for study and research in medical and other sciences. It is expected to be in operation late this year.

The AEC is negotiating a contract with Curtiss-Wright for construction of a large gamma food irradiation facility for the Army at Sharpe General Depot, Lathrop, Calif. The project, scheduled for completion in 1960 at a cost of about 2 million dollars, will be devoted to the preservation of food by irradiation.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1958 Clinical Meeting, Minneapolis, Dec. 2-5.
1959 Annual Meeting, Atlantic City, June 8-12.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.

AMERICAN

July

American Society of Facial Plastic Surgery, New York, July 16. Dr. Samuel M. Bloom, 123 E. 83d St., New York 28, Secretary.

August

American Congress of Physical Medicine and Rehabilitation, Philadelphia, Bellevue-Stratford Hotel, Aug. 24-29. Dr. Frances Baker, 1 Tilton Ave., San Mateo, Calif., *Secretary.*

American Hospital Association, Palmer House, Chicago, Aug. 18-21. Dr. Edwin L. Crosby, 18 E. Division St., Chicago 10, Director.

American Veterinary Medical Association, Sheraton Hotel, Philadelphia, Aug. 18-21. Dr. J. G. Hardenbergh, 600 S. Michigan Blvd., Chicago 5, Executive Secretary.

Biological Photographic Association, Shoreham Hotel, Washington, D. C., Aug. 19-22. Miss Jane Waters, Box 1668, Grand Central P. O., New York 17, Secretary.

Chemical Organization of Cells, Normal and Abnormal, Madison, Wis., Aug. 21-23. Dr. J. F. A. McManus, Univ. of *Alabama Medical* Center, Birmingham, Ala., Chairman.

International College of Surgeons, Regional Meeting, Western Section, The Riverside Hotel, Reno, Nev., Aug. 21-23. For information address: Dr. Leo D. Nannini, 190 Mill St., Reno, Nev.

National Medical Association, Hotel Schroeder, Milwaukee, Aug. 11-14. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Northwest Proctologic Society, Sun Valley, *Ida.*, Aug. 27-29. Dr. John McKay, 645 Medical Dental Bldg., Seattle, Secretary.

Rocky Mountain Radiological Society, Shirley-*Savoy* Hotel, Denver, Aug. 15-17. Dr. John H. Freed, *Denver 20, Secretary.*

West Virginia State Medical Association, The *Greenbrier*, White Sulphur *Springs, Aug.* 21-23. Mr. *Charles Lively*, P. O. Box 1031, Charleston 24, Executive Secretary.

World Medical Association, Copenhagen, *Denmark*, Aug. 15-20. Dr. Louis *H. Bauer*, 10 Columbus Circle, New York 19, Secretary-General.

September

American Academy for Cerebral Palsy, *Sheraton-Biltmore* Hotel, Providence, R. I., Sept. 25-27. Dr. *Raymond R.* Rembolt, University Hospitals, Iowa City, Ia., Secretary.

merican Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 4-6. Dr. E. *Stewart* Taylor, 4200 E. 9th Ave., Denver 20, Secretary.

merican College of Physicians, Mid-West Regional Meeting, Milwaukee, Wis., Sept. 27. Dr. James F. Gleason, 7 S. Oxford Ave., Atlantic City, N. J., General Chairman.

merican Fracture Association, Skirvin Hotel, *Oklahoma City*, Okla., Sept. 29-Oct. 4. Dr. H. W. Wellmerling, 610 Griesheim Bldg., Bloomington, Ill., Secretary.

merican Medical Writers' Association, Hotel Morrison, Chicago, Sept. 26-27. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

merican Roentgen Ray Society, *Shoreham* Hotel, Washington, D. C., Sept. 27-Oct.3. Dr. C. Allen Good, 200, 1st St. S. W., Rochester, Minn., Secretary.

olorado State Medical Society, Broadmoor Hotel, Colorado Springs, Sept. 24-27. Mr. Harvey T. *Sethman*, 1612 Tremont Place, Denver 2, Executive Secretary.

ansas City Southwest Clinical Society, Municipal Auditorium, Kansas City, Mo., Sept. 22-25. Mr. A. L. Bingham, 3036 *Gillham Rd.*, Kansas City 8, Mo., Executive Secretary.

ntucky State Medical Association, Brown Hotel, Louisville, Sept. 23-25. Mr. J. P. Sanford, 1169 Eastern Parkway, Louisville 17, *Executive Secretary.*

ichigan State Medical Society, Sheraton-Cadillac Hotel, Detroit, *Sept. 30-Oct.* 3. Dr. L. Fernald Foster, 606 Townsend St., P. O. Box 539, Lansing, Mich., Secretary.

ississippi Valley Medical Society, *Morrison Hotel, Chicago*, Sept. 24-26. Dr. Harold Swanberg, 510 Main St., Quincy, Ill., Secretary.

Montana Medical Association, Northern Hotel, *Billings, Sept.* 11-13. Mr. L. R. Hegland, P. O. Box 1692, Billings. Executive Secretary.

Nevada State Medical Association, Elko, Sept. 17-20. Mr. Nelson B. *Neff*, P. O. Box 188, Reno, Executive Secretary.

New Hampshire Medical Society, Mt. Washington Hotel, Bretton *Woods, Sept.* 19-22. Mr. Hamilton S. Putnam, 18 School St., Concord, Executive Secretary.

Northeastern Section, American Urological Association, Equinox House, Manchester, Vt., Sept. 12-13. Dr. F. O. Harbach, 831 James St., Syracuse, N. Y., Secretary.

Oregon State Medical Society, Columbia Athletic Club, *Portland*, Sept. 3-5. Dr. Max H. Parrott, 1020 S. W. Taylor St., Portland 5, Secretary.

Texas Academy of General Practice, San Antonio, Tex., Sept. 22-24. Mr. Donald C. Jackson, 1905 N. Lamar, Austin, Tex., Executive Secretary.

Tri-State Medical Society, Shreveport, La., Sept. 18. Dr. J. C. Sanders, Sanders Clinic, Kings Highway, Shreveport, La., Secretary.

United States Section, International College of Surgeons, Atlantic City, N. J., Sept. 7-11. Dr. Karl Meyer, 1835 W. Harrison, Chicago, Secretary.

Utah State Medical Association, Hotel Utah, Salt Lake City, Sept 9. Mr. *Harold Bowman*, 42 S. Fifth East St., Salt Lake City 2, Execu Secretary.

Vermont State Medical Society, Mt. Washington Hotel, Bretton Wo N. H., Sept. 20-22. Mr. Getty Page, 128 *Merchants Row*, Rutland, Executive Secretary.

Washington State Medical Association, Davenport Hotel, Spoka Sept. 14-17. Mr. Ralph W. Neill, 1309 *7th Ave.*, Seattle, Execut Secretary.

October

American Academy of Ophthalmology and Otolaryngology, Pal House, Chicago, Oct. 12-17. Dr. W. L. Benedict, 100 First Avenue Bl *Rochester, Minn.*, Secretary.

American Academy of Pediatrics, Palmer House, *Chicago, Oct.* 20- *Dr. E. H. Christopherson, 1801 Hinman* Ave., Evanston, Ill., Execut Secretary.

American Association of Medical Clinics, Palace Hotel, San Francis Oct. 2-4. Dr. John *R. Hand*, 1216 Southwest Yamhill St., Portla Ore., Secretary.

American Association of Medical Record Librarians, Statler Hot Boston, Oct. 13-16. Miss Doris Gleason, 510 N. Dearborn St., Chica 10, Executive Director.

American Association of Public Health Physicians, St. Louis, O 27-31. Dr. Joseph M. Bistowish, P. O. Box 1117, Tallahassee, Fl Secretary.

American Association for the Surgery of Trauma, Drake Hotel, Cl cago, Oct. 2-4. Dr. William T. Fitts, Jr., 3400 Spruce St., Philadelphia Secretary.

American Clinical and Climatological Association, Otesaga Hot Cooperstown, N. Y., Oct. 9-11. Dr. Marshall N. Fulton, 124 Waterm St., Providence 6, R. I., Secretary.

American College of Gastroenterology, Jung Hotel, *New Orlea* Oct. 19-25. Mr. *Daniel* Weiss, 33 W. 60th St., New York 23, Executi Secretary

American College of Surgeons, Oct. 6-10. Dr. Michael L. Mason, *E. Erie St., Chicago, Secretary.*

American Dietetic Association, Bellevue-Stratford Hotel, Philadelph *Oct. 21-24. Miss Ruth* M. Yakel, 620 N. *Michigan* Ave., Chicago 1 Executive Secretary.

American Heart Association, Fairmont Hotel, San Francisco, Oct. 24-2 *Mr. John D. Brundage*, 44 E. 23d St., New York 10, Secretary.

American Otorhinologic Society for Plastic Surgery, Conrad Hilt Hotel, Chicago, Oct. 12. Dr. Joseph G. Gilbert, 75 Barberry Lane, Rosl Heights, N. Y., Secretary.

American Public Health Association, Kiel Auditorium, St. Louis, O 27-31. Dr. Berwyn F. Mattison, 1790 *Broadway, New York* 19, Secreta

American School Health Association, St. Louis, Oct. 26-31. Dr. A. *DeWeese*, 515 E. Main St., Kent, *Ohio, Secretary.*

American Society of Anesthesiologists, *Penn-Sheraton Hotel*, Pitt burgh, Oct. 19-24. Dr. J. Earl *Remlinger, 802 Ashland Ave.*, Wilmett Ill., Secretary.

American Society of *Plastic* and Reconstructive Surgery, Drak Hotel, Chicago, Oct: 12-17. Dr. Kenneth L. Pickrell, Duke Univ. Hosp Durham, N. C., Secretary.

Association of American Medical Colleges, Ocean House, Swampscott Mass., Oct. 13-15. Dr. Dean F. Smiley, 2530 Ridge Ave., Evanston, Ill. Secretary.

Association of Life Insurance Medical Directors of America, Statl Hotel, Hartford, Conn., Oct. 22-24. Dr. Royal S. Schaaf, P. O. Box 59 *Newark 1, N. J., Secretary.*

Association of Medical *Illustrators*, Dallas, Tex., Oct., Miss Rose M Reynolds, *42d & Dewey Ave.*, Omaha 5, Secretary.

Association of *State & Territorial* Health *Officer*: *Hotel* Wash ington, Washington, D. C., Oct. 22-24. Dr. Mack I. *Stanholtz*, Sta Office Bldg., *Richmond*, Va., Secretary.

Central Association of Obstetricians and Gynecologists, Hot Leamington, Minneapolis, Oct. 2-4. Dr. Edwin J. DeCosta, *104 S.* Mich gan Ave., Chicago 3, Secretary.

Central Neuropsychiatric Association, Deshler Hilton Hotel, Colum bus, O., *Oct.*, 17-18. Dr. Ralph M. *Patterson*, Ohio State Univ., Colle of Med., Columbus 10, O., Secretary.

Central Society for Clinical Research, Drake *Hotel*, Chicago, Oct 31-Nov. 1. Dr. Austin S. Weisberger, 2065 Adelbert Rd., Celeveland Secretary.

Clinical Orthopaedic Society, Brown *Palace Hotel*, Denver, Oct. 2 Dr. *Charles* H. Franz, 1801 Wealthy St. S. E., Grand Rapids, Mich. Secretary.

Congress of Neurological Surgeons, St. Francis Hotel, San Francisco, *Oct.* 29-*Nov.* 1. Dr. Richard L. DeSaussure, 899 Madison Ave., Mem phis, Tenn., Secretary.

Gulf Coast Clinical Society, Pensacola, Fla., Oct. 23-24. Dr. J. J Baehr, Jr., *117 N. Palafox St.*, *Pensacola, Fla.*, *Secretary.*

Indiana State Medical Association, Murat Temple, Indianapolis, Oct 13-15. Mr. James A. Waggener, 23 E. Ohio St., *Indianapolis* 4, Execu tive Secretary.

Pennsylvania, Medical Society of the State of, *Bellevue-Stratf* Philadelphia, Oct. 12-17. Mr. Lester H. Perry, 230 *State St.*, Harrisb Executive Director.

Medical Society of Virginia, Hotel Jefferson, Richmond, Oct. 12-1 Mr. Robert I. *Howard*, 1105 W. *Franklin* St., *Richmond* 20, Execu *Secretary.*

National *Proctologic* Association, Hamilton *Hotel*, Chicago, Oc Dr. George E. Mueller, 59 E. *Madison* St., Chicago 2, Secretary.

Oklahoma City Clinical Society, Biltmore Hotel, *Oklahoma City*, Okl Oct. 27-29. Mrs. Alma *O'Donnell*, 503 Medical Arts Bldg., Oklah City, Okla., Executive Secretary.

Puerto Rico Medical Association, *Santurce*, P. R., Nov. 18-22. Mr J. A Sanchez, Box 9111, Santurce 29, *P. R.*, *Executive* Secretary.

Southwestern Medical Association, *Pioneer* Hotel, Tucson, Ariz., Oct 23-25. Dr. Russel L. Deter, 1501 *Arizona* St., El *Paso*, Tex., Secret

(Continued on page 30)

THE JOURNAL
JULY 12, 1958
VOL. 167, NO. 1

Partners in Progress

Of all the words used in everyday conversation few are more exciting than "progress." This eight-letter word does as much to excite the imagination as any other term, technical or otherwise. One may speak of miracle drugs, atom power, solar energy, and electronics, and audiences think of almost unbelievable developments —but often without any thrill of excitement. Let a speaker, however, mention the possibility of a review of what progress means to the members of an audience, and one can almost hear a stir of anticipation. Somehow this precipitates a train of thoughts that even the most conservative listener finds difficult to hold within nonfanciful bounds.

THE JOURNAL of the American Medical Association is now 75 years old, although in this modern age there is a temptation to use the words 75 years young. It is not four score years old, and yet more significant events have occurred during this time than, perhaps, in hundreds of preceding years. It makes no difference whether one thinks of engineering, medicine, law enforcement, or any other field; the changes that have occurred are so dramatic, so challenging, it is difficult to hink of any corner of the earth, any phase of ife, that is not being affected. And this is only he beginning. What is on the horizon seems even more fantastic to contemplate.

Most of us accept our modern miracles with ittle more than passing wonderment or someimes momentary thankfulness. Often we do not understand; usually we do not appreciate. In act, too often our eyes and our thoughts remain confined to our own fields of interest without realizing how much each field contributes to another, how much each is dependent on another, or how many people and how much training and experience are involved in the various areas of effort.

Elsewhere in this issue of THE JOURNAL are articles from acknowledged leaders in their fields. They are known internationally, and yet they can think in terms of the individual as well as of a nation or of the world. As one reads their writings, there grows a recognition and an appreciation of a fundamental fact: they are all partners in progress. No one could be a symbol for his field if he had stood alone or if his area of interest had been completely isolated from the rest of the community. They served their communities as well as their organizations or businesses and in so doing extended their influence throughout the country and even elsewhere in the world.

The practicing physician likewise serves more than his patient. He is part of community life, and his work influences as widely that of others as they in turn influence his work. No one can exist without the direct or indirect contributions of others, which is forcefully proved by the appearance of our guest contributors in the pages of this issue of THE JOURNAL. Physicians as well as our guests know this, but do others, especially those who are quicker with criticism than with thoughtful suggestion? Maybe the latter might be made candidates for the development of the theme "Partners in Progress." An explanation here, an example there, might be sufficient to change the misunderstanding critic into a helpful ally. If the people of the United States believe in the principles on which this nation was built, they must demonstrate a willingness to insist on the continuation of these principles. Leadership is necessary, but understanding is as important. Who can better provide the explanation and the examples than such men as our guest contributors and the many others who are acknowledged in their fields?

Writer, news commentator, industrialist, educator, name whom you will, are all partners in living in our country. This in itself engenders a depth of responsibility that is sobering, but when one remembers that much of the world today is looking for leadership, all of us must be mindful of additional responsibility as we work and play. Perhaps the people in some of the countries elsewhere might have had fewer problems if they had paused long enough in their work and play to encourage men and women to shake hands with each other as partners in orderly progress. Maybe there would be less fist shaking today.

Austin Smith

THE WHITE HOUSE
WASHINGTON

April 9, 1958

Dear Dr. Smith:

It is a privilege to extend felicitations to the Journal of the American Medical Association on its 75th anniversary.

I have long been aware that the Journal has, throughout its lifetime, been a potent force for progress in the field of medical discovery and medical information. The contribution its editors make to medical advancement is reflected daily in better health for the people of this country and the world.

Throughout my lifetime of service in the Army, as well as in my present position, I have watched with pride and interest the giant strides that have been achieved toward a rising standard of health for people everywhere. The Journal of the American Medical Association has reported these advances faithfully, and its editors must share with me both a sense of deep accomplishment and the conviction that in the years to come the horizons are truly unlimited.

With best wishes to you and to the Journal,

Sincerely,

Dr. Austin Smith
Editor
Journal of the American Medical Association
535 North Dearborn Street
Chicago 10, Illinois

Medicine and the Community

Gunnar Gundersen

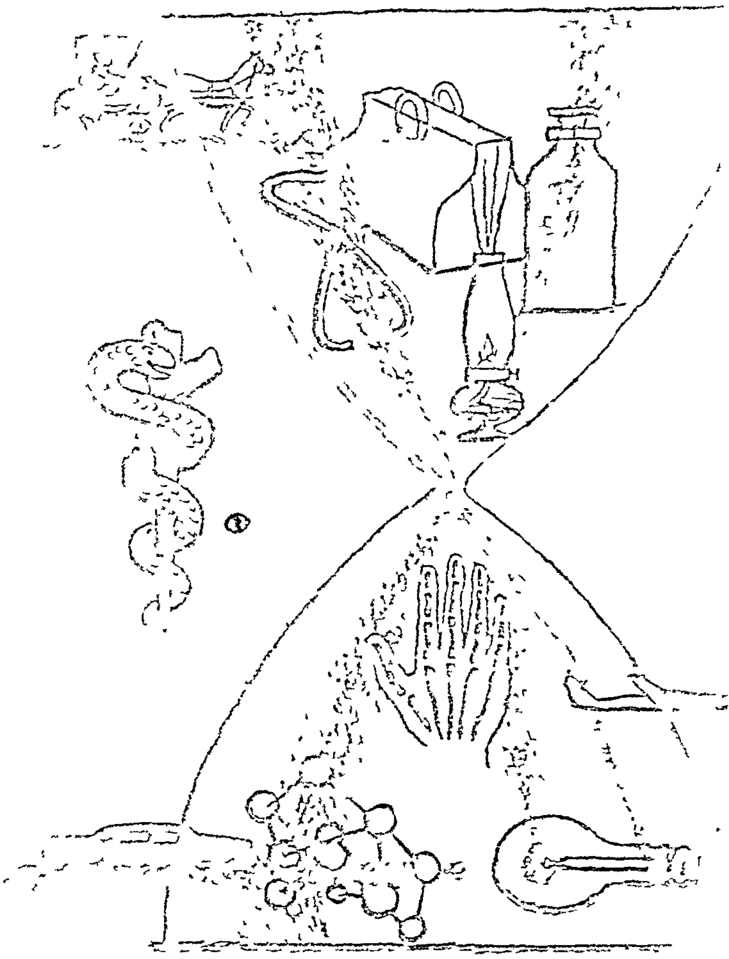
When The Journal of the American Medical Association began publication in 1883, medicine was entering a dramatic era of scientific progress which has accelerated down through the years and which continues today at an ever faster pace. Although medical knowledge is a widening, deepening river, formed from the streams of work and observation by countless thousands of people over the centuries, the fact remains that medical science has advanced more in the past century than it had in the previous 3,000 years. This advance has been especially rapid and dramatic since the turn of the century.

There were, of course, numerous historic milestones prior to the quickening developments of the period 1850-1900. Already accomplished, for example, were the discovery of the ligature for controlling hemorrhage, Harvey's observations on the circulation of blood, the conquest of scurvy, the discovery of smallpox vaccine, and the inventions of the stethoscope and microscope. A great deal of basic knowledge had been accumulated in such fields as anatomy, physiology, the cellular structure of body tissue, clinical descriptions of disease, and techniques of physical diagnosis. Advances in biology, chemistry, and physics were providing new tools, and socioeconomic changes stemming from the Industrial Revolution were giving added stimulus to scientific and medical progress.

So, during the last half of the 19th century, the stage was set for the exciting drama that unfolded. In the years just before and after the founding of The Journal, some giants were at work, leaving an indelible impress for humanity and medical history. Virchow and his successors in the field of pathology were making the monumental discoveries which for the first time in history provided a sound concept of disease and paved the way for modern medicine and surgery. Pasteur, Lister, Koch, and the many other so-called microbe hunters were bringing the mysterious out into the open, by revealing that bacteria and other living organisms cause infectious disease. Patrick Manson, Theobald Smith, and Walter Reed were showing that many diseases are transmitted by insects, parasites, and other animals. Twelve years after THE JOURNAL began publication, Roentgen discovered the x-ray and thus opened new vistas in both diagnosis and treatment.

THE JOURNAL was born at an exciting time in medical history, and ever since then it has played a leading role in transmitting new medical knowledge to the physicians of America and the world. Around the turn of the century, and in the years following, the great Sir William Osler correlated the growing mass of knowledge into an exact clinical application of diagnosis and treatment. During the first quarter of this century new attention was being paid to such things as nutrition, metabolism, glandular functions, and the general field of body chemistry. Dramatic discoveries were made in connection with the cause and treatment of diabetes, pernicious anemia, and other noninfectious diseases. At the same time, rapid progress was being made in public health and sanitation, disease prevention through immunization and quarantine procedures, the development of specific drugs for treatment, continued refinements in surgery, anesthesiology, and obstetrics, the radical improvement of American medical education, and the constant upgrading of hospital facilities and standards of care.

Despite this exciting march of medical progress up to about 1925, the advances of the past 30 years have been even faster, more dramatic, and certainly more difficult to keep up with. An amazing number of words, terms, techniques, and products which today are commonplace in our medical vocabulary did not even exist only three decades ago. Everyone, of course, is familiar with the tremendous impact of the so-called wonder drugs, the sulfonamides and antibiotics, against pneumonia and other bacterial infections. New chemicals have been introduced to combat tuberculosis, malaria, and high blood



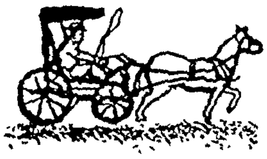
pressure. Anticoagulants and liver extract, unknown 30 years ago, are in common use today. As a result of advances in the field of endocrinology, various hormones have been identified and synthesized for use against arthritis and other chronic ailments.

Antihistamines have become valuable tools in the field of allergy. Tranquilizing drugs and other new forms of chemotherapy are aiding the fights against mental disease and alcoholism. Vitamins, just gaining recognition a generation ago, have greatly reduced the extent of deficiency diseases and have helped improve the general nutrition of our people. New knowledge of the human blood has brought dramatic lifesaving techniques. Blood transfusions, used sparingly three decades ago, are commonplace today. Blood banks have been established all over the country to assure an ample supply of *whole blood* and its various components. Plasma and *dried plasma* are being widely used. *Replacement transfusions*, which provide a complete *new supply of blood*, are now being used to save the lives of infants with certain abnormal blood conditions. Recognition of the Rh factor and the discovery of different types of hemoglobin have opened up entirely new fields of blood research.

A generation ago many people thought that surgery had just about reached its peak, and they predicted that the future could bring little more than the refinement of operating techniques. Today, however, we are witnessing surgical operations which were considered impossible only 10 or 15 years ago. For example, surgeons are repairing various types of congenital and acquired heart lesions, removing entire lungs, replacing segments of blood vessels with grafts or synthetic substitutes, and transplanting corneas from one eye to another. They are being helped in very great measure by notable advances in the knowledge and administration of anesthetics; the giving of blood, other fluids, and antibiotics; the use of low temperature procedures; the artificial heart, lung, and kidney machines; bone graft banks; eye banks; and blood vessel banks. Meanwhile, surgical patients are being put on their feet sooner than they used to be. This not only has improved and speeded postoperative recovery but also has insured a faster turnover *in occupancy* of hospital beds.

Thirty years ago the science of virology was in *its infancy*, but now it is reaching an age of rapid development. An increasing number and variety of viruses are being recognized, isolated, classified, and grown in laboratory cultures. Their *relationship* to specific diseases is being studied and determined. The development of the poliomyelitis and influenza vaccines has blazed the trail for new studies which give promise of reducing the toll from many other ailments caused by viruses. Numerous cancer research workers are investigating the possible relationship between viruses and malignant growths, and there are indications that they may be on the verge of important findings.

All of this, plus much more that I have not included, would be of interest only to students of medical history had not the constant stream of knowledge been translated into practical methods of examination, diagnosis, treatment, and prevention—for the everyday use of practicing physicians in their communities. The scientific progress has been accompanied by many other developments affecting both doctors and patients—the growth and increased utilization of *hospital facilities*; the increase in specialization; the evolution of *clinics*, *medical centers*, and various forms of *group practice*; the remarkable development of voluntary health insurance, especially in the past 10 years; the steady growth of public health activities; the rise of the national voluntary health organizations; the public's mounting interest in health and disease; the federal government's increasing activity in the fields of medical care and medical research; and many other socioeconomic factors involving the organization and financing of medical services.



Keeping pace with the ever changing complexities and problems of medicine, the American Medical Association down through the years has steadily expanded its activities to serve both the profession and the public. For example, the first *scientific exhibit* was presented in 1899; today, a typical A. M. A. annual meeting features almost 700 scientific and technical exhibits which make up just one part of a huge, five-day postgraduate course. Starting in the years just after the turn of the century—and I am giving only a few chronological highlights—the Association formed councils, bureaus, and committees to study and disseminate information in such *fields as standards of medical school and hospital training*, evaluation of new pharmaceutical products, the operations of quacks and cultists, public health education, legal medicine and legislation, medical appliances, foods and nutrition, the costs and distribution of medical services, the health of industrial workers, the effects of social and economic changes on medical practice, rural health problems, medical motion pictures and television, public relations, national defense, federal legislation, mental health, alcoholism, the problems of aging, and the medical aspects of hypnosis.

* * *

This list, which is far from complete, helps to illustrate the changing medical picture and the fact that modern medicine cuts across all phases of community life. Whether one is thinking in terms of maternal and infant care, a child in school, a boy on an athletic field, a worker in a factory, a farmer in the field, a draftee in the armed services, a housewife in the kitchen, a community health problem, a drunk on the corner, poliomyelitis immunization, Asian influenza, or the need for an effective poison-control center, the profession is doing something about the medical aspects of the problem, and it stands ready and able to help others who are interested.

Modern medicine has progressed over the years not simply through its own efforts but also by virtue of the help and cooperation given by many segments of American life—industry, labor, education, private philanthropy, the great foundations, government, and, above all, the general public. Today, more than ever before, medicine is interdependent with the business and economic life of the nation and is caught up in all the countless cross-currents of public interest, public opinion, and political action. This creates a variety of problems arising from different viewpoints and ideologies, but it also presents many challenging opportunities for leadership, cooperation, and understanding.

The medical progress which I have sketched only briefly has made drastic cuts in the incidence and death rates of many diseases which once were serious health problems. It has increased the average life expectancy at birth almost 23 years since 1900. Over the same time span the proportion of people 45 years of age and older has risen from 18% to 29%. As a result, medical emphasis is shifting from the infectious, communicable diseases to the chronic or degenerative diseases which take their greatest toll in later life—heart disease, arteriosclerosis, high blood pressure, cancer, arthritis, and similar ailments. Increased attention also is being given to neurological diseases, mental illness, emotional disorders, and respiratory ailments, such as the common cold, hay fever, asthma, and sinusitis.

The future will see even greater emphasis on disease prevention, maintenance of good health, and effective rehabilitation of the disabled. Technological advances, aided in great measure by new developments in electronics and atomic medicine, will reveal a multitude of facts concerning cardiovascular diseases, cancer, mental and nervous disorders, and various chronic ailments. An increasing proportion of medical services will be provided through clinics, medical centers, and various types of group practice. There will be interesting new developments in the design and operation of hospitals. Voluntary health insurance, if it is not destroyed by government ventures in compulsory health insurance, will solve the problem of medical care costs for all the people of the United States except the indigent. The latter, as always, will be taken care of by private and public charity, and it may be possible that plans for the indigent also will be financed on an insurance basis.

The future of American medicine is bright, if we can continue to work in an atmosphere of freedom, motivated by the dual spirit of enterprise and cooperation. The dominant socioeconomic challenge of the present is to preserve that atmosphere and that spirit.

Gunnar Gundersen
President of the American Medical Association

American Chemical Industr

During my lifetime—and I am a good many years younger than THE JOURNAL of the American Medical Association—there has been a spectacular evolution in industrial chemistry, particularly in the United States. In addition to the fundamentals of demand and supply, I believe that my industry's growth has been affected by two unusual factors. The first is the remarkable attraction it has exerted for restless people who are dissatisfied with the way they find things on this earth. They want to change them for the better. The second is that those people have been unusually quick to seize not only upon chemistry's own discoveries but also upon the advances achieved in most other fields of human endeavor. Here I will mention only chemical engineering, electrical engineering, mechanical engineering, biology, education, forestry, medicine, veterinary medicine, geology, business administration, accounting, psychology, law, mathematics, and public communications. There are many others.

It can fairly be said that until the time of World War I the world was dominated by the foreign chemical industry. Before those days, the United States had little or no tariff protection, and a lot of people in this country wanted little or no part in such protection. I credit three tariff laws—the Payne-Aldrich Act of 1909, the Underwood Act of 1913, and the Fordney-McCumber Act of 1922—with setting the stage for the development of the chemical industry in this country.

Chemical manufacturers were compelled to fight the British bleaching powder cartel and the German bromine cartel in the earlier years of this century. These wars—and they were wars—would not have been necessary if our industry had been given the protection it so sorely needed when it was striving to get off the ground. Let us hope there will be more alertness to providing protection, where deserved, in the future than there has been in the past.

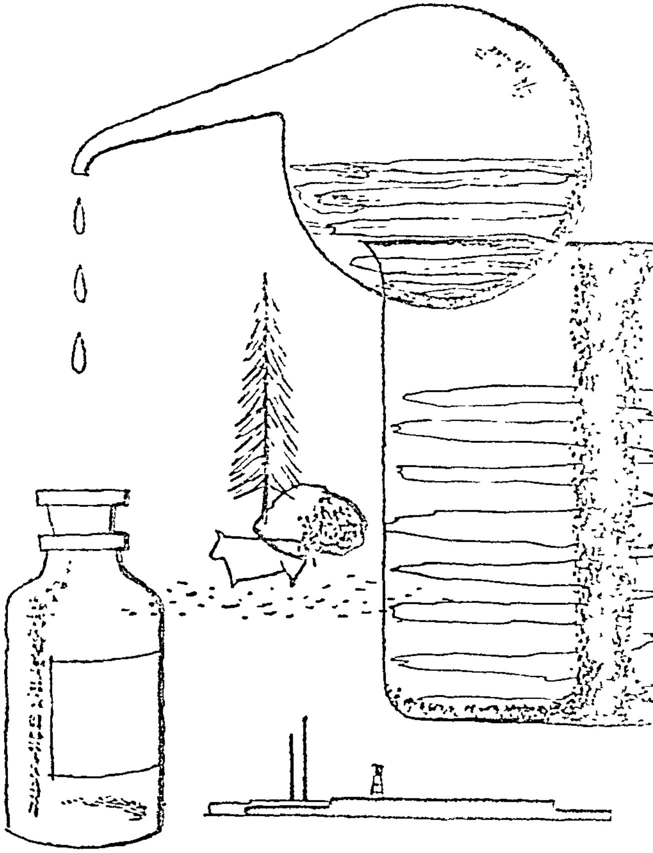
European domination of the American market was one fact of life which all of the early chemical companies had to face. However, enterprising Americans with the will to compete had developed a chemical industry of sorts from colonial times. Yet, even as late as 1880, the chemical industry occupied only a minor place in the industrial life of our country. It employed 10,000 persons, had an investment of 25 million dollars, and sold some 35 million dollars in goods annually.

By 1914, employment was 32,000, investment was 225 million dollars, and sales came to 160 million dollars. Four years later, these figures had been multiplied approximately threefold. Sales totaled about 500 million dollars. They reached this then-enormous figure because of World War I. But today, each one of the top five American chemical companies equals or exceeds 500 million dollars in annual sales.

In the United States now, there are about 12,000 chemical plants manufacturing in the neighborhood of 9,000 different products in commercial quantities. The industry employs well over one million people, has an investment which exceeds 35 billion dollars, and has annual sales topping 25 billion dollars.

During the early 19th century, the industry was devoted almost entirely to the extractive methods of chemistry. In the latter part of the 1800's, the industry entered the reactive phase, and this was soon followed by the synthetic phase. During this latter period, the chemist was faced with the problem of gaining acceptance of synthesized products as being equal to or better than products derived from natural sources. Was wintergreen oil produced from natural sources better than methyl salicylate, or vice versa?

About this time an interesting case got into the courts of law. A soft-drink manufacturer was accused of adulterating his grape drinks by



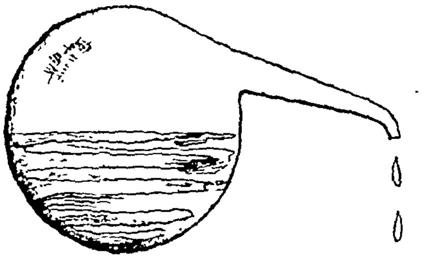
adding methyl anthranilate, a synthetic grape flavoring. Upon analysis, the drinks were found to contain methyl anthranilate. The expert chemist who was called as a witness so testified, but, when asked by the judge who had added the chemical, he replied, "God put it there, since all grape juice contains methyl anthranilate." Now synthetics are widely accepted, often as improvements upon natural substances, but this was not always so.

The U. S. Census report of 1880 noted the limited production of alkalis in this country. But one year after THE JOURNAL was founded, an ammonia-soda plant was built at Syracuse, N. Y. A soda-ash plant was in operation in Michigan in 1895. Bleaching powder was being commercially produced in Virginia in 1896. About the same time, electricity was being used to produce bromine and chlorine from Michigan brines. Elemental phosphorus production via the electric furnace began at Niagara Falls in 1897. The next year calcium carbide production began by electric furnace reduction. Meanwhile, Herman Frasch conceived his idea of mining underground sulfur with live steam, and within a few years America led the world in producing sulfuric acid. In 1909, with use of a European process, fixation of atmospheric nitrogen was being performed at Niagara Falls, N. Y.

An interesting aspect of chemistry in the early 1900's was that it was using designs and equipment developed by the mining industry. Today chemistry is still being advanced through the contributions of mining and metallurgy. Steel, chromium, manganese, vanadium, molybdenum, titanium, nickel, cobalt, copper, and many other metals and their alloys made it possible to develop the materials which can withstand the pressures, temperatures, and corrosions of newborn chemicals.

But many chemists can easily remember when chemicals were being produced by batch processes in such equipment as stoneware crocks, glass carboys, and enameled bathtubs. Aspirin was first made in bathtubs. The crystals were ladled out of the mother liquor with wooden scoops and then washed and dried in centrifugal laundry dryers lined with canvas bags. The bathtubs were cheap and served the purpose, since no other apparatus was available.

Until World War I, the American chemical industry dealt largely with inorganic chemicals. Germany was recognized as the country of chemical research and chemical knowledge, particularly in the organic field. In July of 1916, a cargo of dyes and other chemicals arrived in Baltimore on board the German submarine "Deutschland." The same submarine brought a second cargo to New London, Conn., in November of 1916. On April 6, 1917, the United States declared war on Germany. These, then, were the last shipments to arrive from the chemical empire of the world. We were left stranded. Or were we?



Quietly, and built upon daring and often impatient research, the American industry was about prepared to start leapfrogging in organic chemistry. In December of 1916, one chemical company succeeded in synthesizing indigo. Others entered the coal tar dye business at about the same time. When Spindletop blew in in 1901, no one foresaw the influence of the oil industry on the chemical industry. It was not generally recognized at the time, but the raw materials for petrochemistry were assured. This was the beginning of a new era.

Now the United States is producing thousands of organic compounds, many of them discovered in early research but simply shelved or remaining unrecognized until society advanced to "catch up" with them. In this connection, it is somewhat entertaining to recall that, in 1914, a chemical company was finding it very difficult to produce a chemical called monochloromethyl acetate. A "bug" in the process resulted in the formation of a then-worthless substance known as vinyl chloride. The chemists went to a lot of trouble to eliminate this substance, which today is accorded considerable respect as vinyl plastic. Many chemical companies can cite similar instances in their history.

Early in this century, chemical research began changing. The lone chemist, who, sometimes with the assistance of a helper, discovered something and painstakingly began developing a way to make it in larger and larger batches, has been replaced by systematic effort in chemical company laboratories.

The last two decades have seen great developments in research methods and techniques of bringing all the necessary technical specialties to bear upon the problem at the same time. Experimental work, materials handling, equipment design, and manufacturing techniques are approached simultaneously as parts of one package. The results can be seen not only in new products, new processes, and new applications but also in the staggering growth of the industry.

Until about World War II, natural gas was a nuisance to the oil producer. If a driller struck gas, the well was promptly capped and abandoned. The gas which propelled the oil to the surface was separated at the well—the oil pumped to storage, the gas vented and flared and wasted forever. You could read a newspaper by the light of flares while driving at night in almost any direction out of Houston.

In the 1930's, the flares began going out. The full significance of Spindletop was being recognized as the Gulf Coast petrochemical industry began developing. Before that time, organic chemistry had largely been based upon coal tar.

Now the ethylene and propylene made from the former waste products of the petroleum industry are building blocks for a wide range of chemicals, such as glycols, alcohols, styrene, and polyethylene. Methane, or common cooking gas, is the mother of a whole family of useful solvents and acetylene products. Discoveries still undreamed of will yet be made.

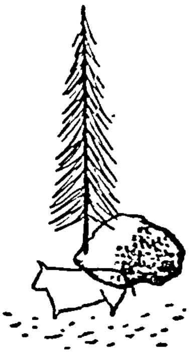
The breakthrough in the American chemical industry was paced by the development of new tools and instruments to measure, record, and control chemical reactions. The pH analyzer and recorder and the oxidation potential analyzer and recorder opened up new methods and means of chemical production. They were only the forerunners of many analytical and controlling devices which are rapidly leading us to automatic operations in the fullest sense. Not too far in the future, we can expect to see computers handling the job—preparing the optimum operating conditions and controlling the operations automatically.

We who have lived through the past 50 to 60 years have been most fortunate to have seen the developments of this fabulous period. Our standard of living has been improved by development after development. Water and sewage treatment with chemicals has made modern urban society possible. Food production via fertilizers and insecticides has pushed the Malthusian theory back a few centuries. Chemical feed supplements, vaccines, pesticides, and veterinary medicines for cattle and other animals have cut diseases to a minimum. Since 1935, when the sulfonamides were introduced, and the 1940's, when penicillin was made widely available, the use of chemotherapy has in many hundreds of thousands of cases caused death to take a holiday.

In the fast-moving chemical industry, knowledge has been accumulated at such a pace that the college senior of yesteryear sees the freshman of today using his textbook. Soon colleges must face up to the fact that they must extend their courses to five years or more in order for their graduates to prepare themselves adequately for the problems they must face and solve in industry.

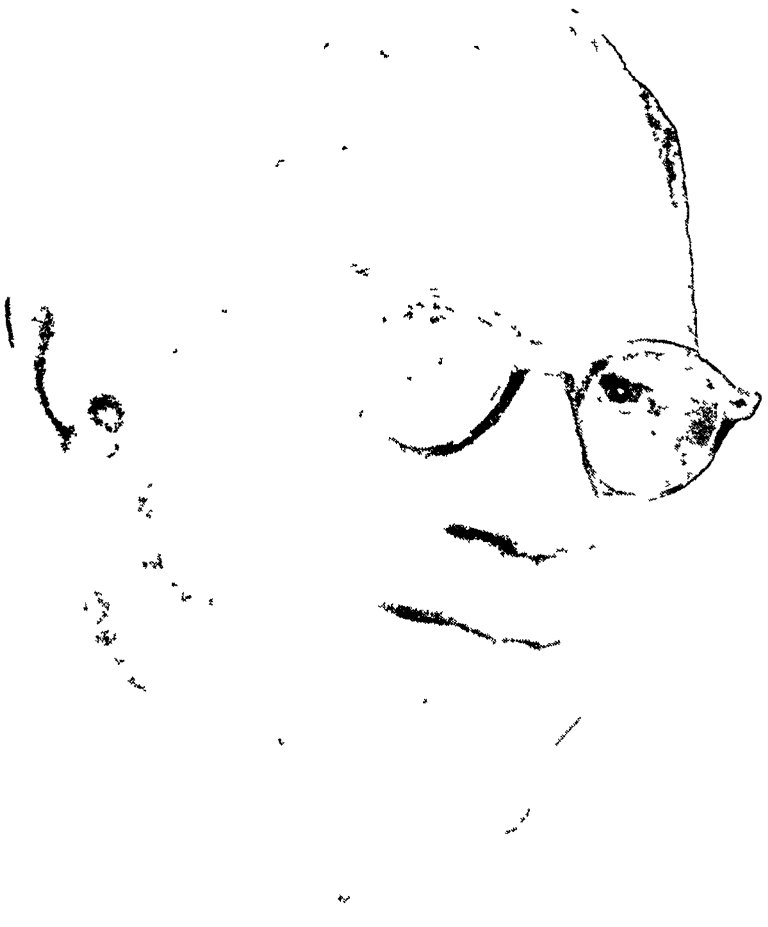
Even so, the educational process does not stop when the sheepskin is framed and hung. There is no marking of time or pausing for breath for those people who intend to change things on this world. In chemistry, as in medicine, the "changers" provide something new, something of interest, each day, each week, each month.

A. P. Beutel
Vice-President of the Dow Chemical Company
and General Manager of its Texas Division



Good Medicine for Industry

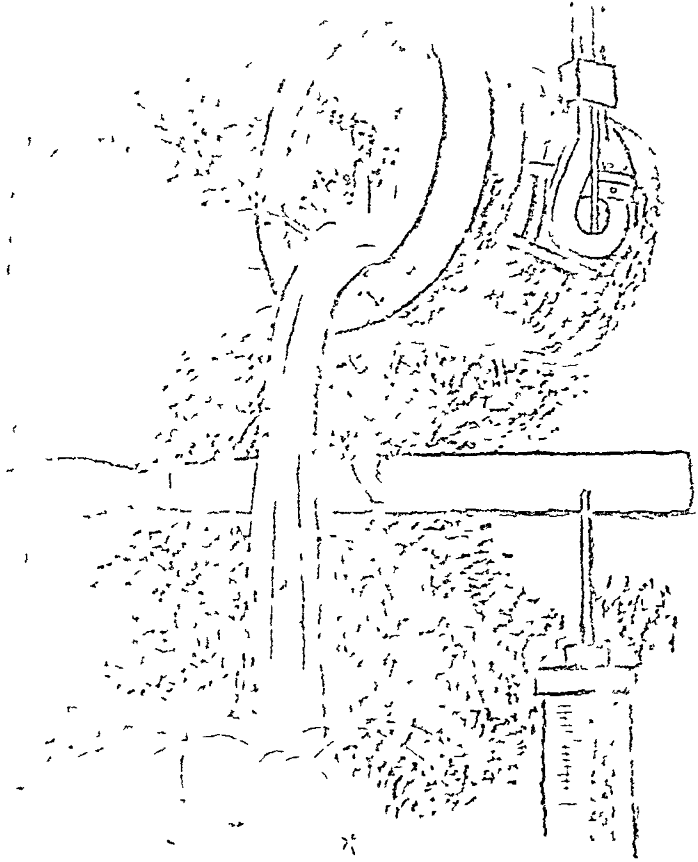
Roger M Blough



In the 75 years since The Journal was first established, the United States has completed the transition from an agricultural to an industrial economy. It is this change that has given us a standard of living unparalleled in the world today. Our leadership in world affairs has stemmed in considerable measure from the phenomenal development of our industrial productivity.

Modern steelmaking began in this country with the introduction of the Bessemer process about 100 years ago and of the open hearth furnace about 90 years ago. So large-scale production of steel in America is very little older than The Journal. The intervening years have produced a tremendous increase in the per capita use of steel. In the past 75 years, steel capacity has risen from 556 lb. per person to almost 1,600 lb. per person. These same 75 years have produced a tremendous increase in medical knowledge and in diagnostic and treatment techniques.

In the years following the passage of the first Workmen's Compensation statutes in 1911, large industries, and especially heavy indus-



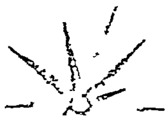
tries, recognized the need for doctors and nurses in their plants to furnish readily available, competent care for injured employees. In addition, preemployment examinations were begun to assure that an applicant was physically suited for the job.

In the ensuing years there developed, through a combination of engineering and medical knowledge, the science of industrial hygiene and toxicology—its purpose has been to assure a healthful work environment in industry. Through a study of air contaminants and other potentially harmful agents in the plant, this science has made it possible for industry to make use of the many thousands of chemical and physical agents with which it now deals, without harm to employees.

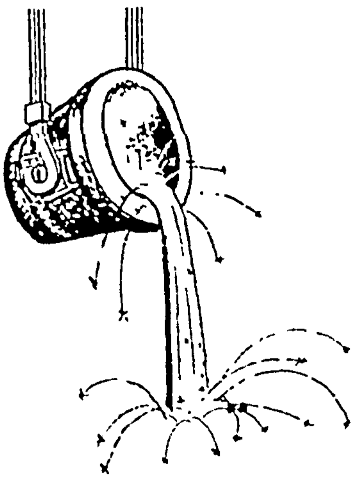
World War II furthered the beginnings of a significant change in medicine's service to industry. In that struggle for survival the productive capacity of every individual was needed to produce the tools of war. Out of that experience it became apparent that there were ways in which preventive medicine could assist in maintaining and improving the health and, hence, the productivity of people at work. A number of industries, including United States Steel, are involved in a realignment of their medical programs to make use of this newer knowledge.

No longer will the sole, or even the *primary*, objective of industrial medicine be the treatment of injuries. Regrettably, there are still industrial injuries to be treated. However, the safety movement in American industry has produced a marked change in the incidence of industrial accidents. In the U. S. Steel Corporation, the lost-time accident frequency rate has been reduced over 95% since 1912. We are proud of the fact that in 1957 the frequency rate in the steel producing divisions was 1.31. Our goal is an accident frequency of zero. Today a steel mill in this company is a much safer place to be than the home or the highway, and this is true of almost all of the large industries and most of the small ones in the United States.

These newer industrial medical programs are primarily preventive in nature. Beginning with a placement examination, they follow the health



of the individual at work. Through health education, medical counseling and guidance, attention to the effect of the work environment on employee health, early disease detection, referral to the family physician for definitive treatment, and follow-up of the man on the job, they bring to the individual employee an effective form of health supervision and guidance that works closely and well with the family physician. Such developments in industry have the sanction of organized medicine and are entirely in keeping with the code of ethics of the medical profession. In 1955, the American Medical Association set up a certifying board to recognize physicians who have special competence in this relatively new field of industrial medicine. Last year, the House of Delegates of the American Medical Association officially endorsed a statement outlining the scope, objectives, and functions of occupational health programs. Thus, as industry and medicine have grown in size and competence, they have also grown closer together.



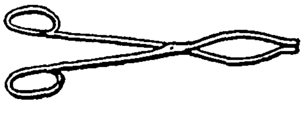
There is another relationship between industry and medicine that has grown rapidly in the last two decades. I am told that over 100 million people in the United States now have some form of prepaid hospitalization insurance. Prepaid coverage of other aspects of medical care has also been growing rapidly. A significant majority of this represents coverage through industrial group insurance plans. In most of these plans industry pays a part, usually half, of the cost. This is true in my company, where the group insurance plans are designed on the 50-50 principle. Last year, employees of this company or their families received $32,400,000 for benefits other than life insurance under these plans, and a major portion of this amount was directly related to doctor and hospital bills.

One can foresee an increasingly close relationship between medicine and industry. New technology will produce new potential health hazards that will need to be evaluated and controlled. But perhaps even more significant is the recognition of the importance of the individual in the production scene. Not only is physical well-being important to full, individual productivity, but mental health as well. We are aware of the impact of emotions on safety and production and of the problems that interpersonal relationships in industry can produce. Doctors are unique in that their entire career is devoted to the study of the individual. One of the functions of the physician is to assist his patient in understanding himself and his relationship to others, in understanding his motivations and his reactions to his environment. The physician is a logical source to turn to for assistance in the search for mental health in industry.

Industry also needs from the medical scientists knowledge of the degenerative diseases and cancer, which daily take their toll at all levels in the industrial structure. Superb progress has been made in the prevention and treatment of infectious diseases. But the coronary attack continues to fell men whose talents and experience are so valuable. It is the fond hope of all that we will one day understand these processes and know how to prevent them. This hope is supported by the great strides in medical knowledge in the recent past.

This progress augurs well for the future and points to an increasingly close relationship between industry and medicine. We should see to it that such relationships carry full recognition of the dignity of the individual, and have as their single goal the health and well-being of industrial America.

Roger M. Blough
Chairman of the Board of the
United States Steel Corporation



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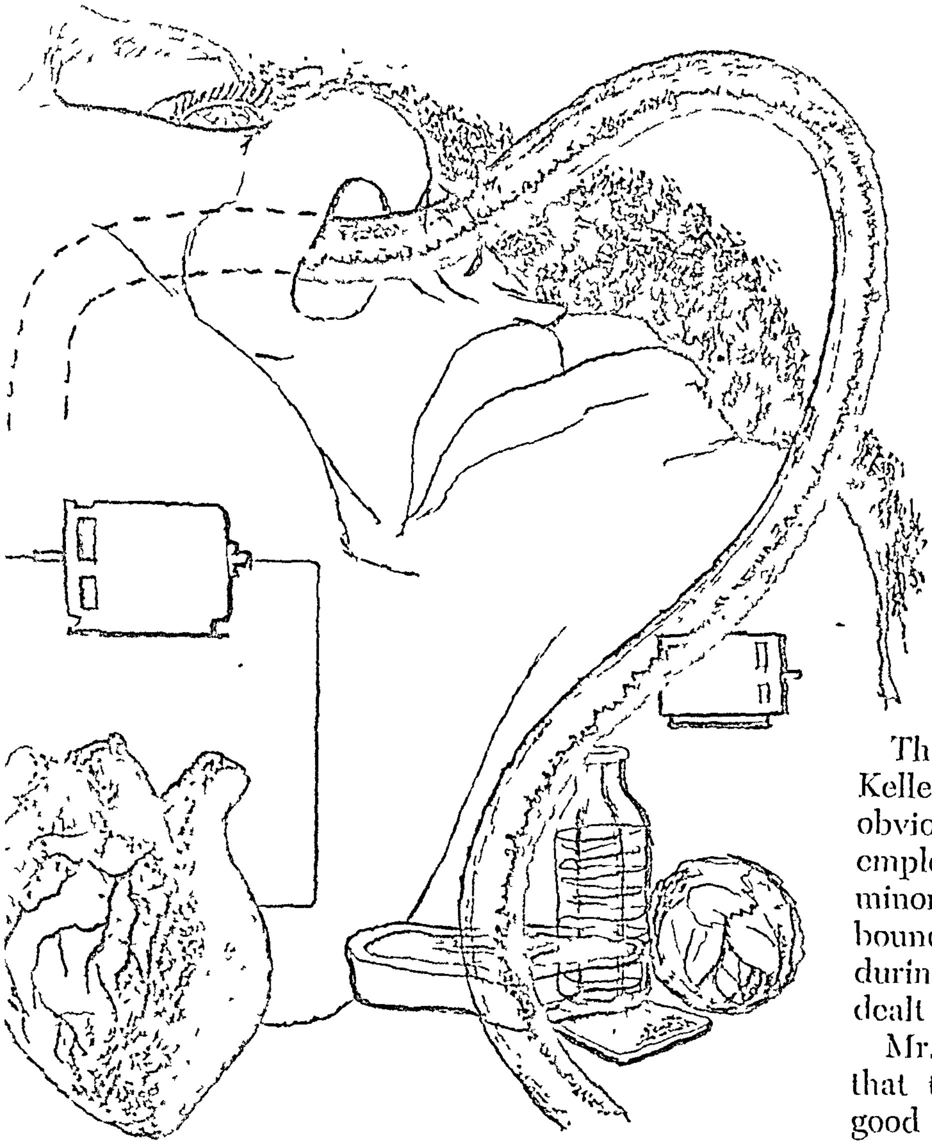
Bitters.—The following official investigation and decision [from the Treasury Department] concerning articles called "bitters," but composed chiefly of alcoholic drink, is worthy of permanent record. Clifford Richardson, Esq., assistant chemist of the Agricultural department, has done me the favor to make a careful analysis of a bottle of the "bitters," and finds it to contain as follows: Absolute alcohol, 32 per cent, Water, 64 per cent, Extracts, only, 4 per cent. He says it is made from a strong alcoholic liquor flavored with various essential oils, as oil of anise, coriander, etc., and contains some vegetable bitters, such as gentian, cinchona, etc. It will be seen that the bitters contain at least 65 per cent. of proof spirits, which will be equal to about 82 per cent. of ordinary whisky at 80 per cent. proof, obviously much more spirits than is absolutely necessary to hold the other ingredients in solution. Containing, as it does, no deleterious drugs and only 4 per cent. of anything like a drug, I should probably be entirely justified in deciding outright that one who sells it for any purpose is a retail liquor dealer.... The department is of opinion that, notwithstanding they may be classified under the internal-revenue laws as medicinal bitters, they should be excluded from Alaska under the executive order of February 4, 1870, forbidding the importation of distilled spirits into that Territory. The courts have decided that certain bitters, substantially similar in character, imported into the United States are dutiable as distilled spirits. You will take action accordingly, and in future seize importations of such bitters into Alaska, and dispose of them in the usual manner. [From the Collector of Customs, Sitka, Alaska] Should I hold it to be a medicine, I should probably do violence to an almost irresistible tendency of the mind to conclude that no genuine medicine needs so much whisky and so few drugs in it, unless under very unusual circumstances. On the other hand, should I decide that it is no medicine at all, I would be confronted by a ten-year' quasi recognition by this office to the contrary, as well as by the practice of many people who use it as such.—Miscellaneous, THE JOURNAL, vol. 1, Sept. 8, 1883, page 281.

Asthma.—Asthma is proverbially considered to be the most intractable of all diseases. Indeed, so uncertain is the effect of any remedy in its treatment, in different individuals, that physicians not unfrequently depend more on the experience of the patient respecting any particular remedy than upon the logical administration of remedies to meet the symptomatic indications. This capriciousness of asthma has led to the most diversified views as to its etiology and pathology, which to the present time has been the most imperfectly understood of any disease with which we are so familiar. Since the time of Laenneck, numerous theories have been proposed to explain the cause and phenomena of the disease, but none have met with more general acceptance than the one proposed by Laenneck himself, that asthma is a neurosis, and depends on either a functional or an organic change in the nerve centers, producing a spasm of the bronchial muscles, and consequent narrowing of the tubes during the attack. This theory of the nervous origin of asthma is founded mainly on the assumption that diseases which cannot be traced to organic lesion, are manifested in symptoms of derangement of the nervous system. . . . [It has been known that] derangement of various organs and disease of various parts of the body would provoke attacks of asthma, and disease in one part or organ will cause, through the agency of the sympathetic nervous system, derangement in another organ, even in remote portions of the body.—John O. Roe, M.D., THE JOURNAL, vol. 1, Sept. 5, 1883, page 295.

Sanitary Science.—Without obedience to the laws of health, it is impossible to secure the highest culture of the citizen—physical, moral and intellectual—and perpetuate the prosperity, freedom, and glory of the State. ... Sanitary science, therefore, is a segment of political economy, and should receive encouragement by the State as a wealth-creating factor—riches, indeed, to the whole people far above that of any other earthly value. It has become a classic saying that "public health is public wealth"; but who can estimate it rightly? Every case of sickness and the loss of every life from preventable disease is a tax upon the material wealth of the State and a great sorrow to the family. Count the number of deaths in a community for any given period, multiply it by thirteen—the estimated number of sick on hand for each death—and you have the average total of sick persons cared for at an expense much greater than would have been necessary for their support in health. In addition to this estimate, let us remember that at least one third of all the cases of sickness and of the deaths that occur are preventable; that this suffering and continuing tax on health and life is in direct antagonism to industry and the general prosperity; that the visitation of diseases falls heaviest always on the poor and most helpless classes of the community; and that the pressure of bad health and poverty, with their far-reaching ill effects upon the growing and reproductive parts of the population, tends to deterioration of the race. In times of epidemic visitation, all these ill influences culminate in general distress of the people.... Finally, in exerting my efforts in advocacy of the cause of sanitary progress, I should commit a serious blunder if I neglected to bespeak the assistance and co-operation of the ladies. Women gave Massachusetts the first State Board on Health in the United States, and from that beginning—in 1869—twenty-eight States have followed the example. There is yet much work for her to do, and none can do it as well as she; and no cause possesses a stronger claim upon her sympathies and affections. As science advances, she gradually acquires her true position in the scale of social life. Of the world's inhabitants, 750,000,000 universally hold woman in a state of bondage and degradation; 250,000,000 alone allow her to approach her proper sphere by acknowledging the marriage contract, paying deference to her influence, and promoting her intellectual culture.—James E. Reeves, M.D., THE JOURNAL, vol. 1, Dec. 1, 1883, page 612.



The Docto Automobile

Back in the early '20's, a young automobile executive named K. T. Keller and a close friend, a family doctor, were talking about the kind of medical care received by industrial workers of that time. Both thought the situation left much to be desired.

If a man hurt a finger or got some foreign matter in an eye, it was the practice of the time to find a doctor in the neighborhood of the plant who could give the man whatever immediate attention he required. The plants were not very well organized to deal with such situations or even, in most cases, to supply adequate first aid, and so treatment could not always be provided quickly enough to avoid complications or unnecessary suffering. Little, or nothing at all, was done for the worker who developed a headache or otherwise became ill during his working day. He had to either endure his aches until quitting time or go home.

This situation seemed unnecessary to Mr Keller and his doctor friend. It seemed to them obvious that the most contented and productive employee was a healthy employee and that even minor illnesses occurring during a shift were bound to affect a man's work. Urgent illness during work, as at any other time, ought to be dealt with promptly and skillfully.

Mr. Keller and his doctor friend concluded that there was no reason why adequate and good medical care could not be provided in manufacturing plants by doctors and nurses employed by the companies on a full-time basis There was no reason, either, why these doctors and nurses should not be highly qualified in their fields—men and women who lived up to the highest medical standards. Also, there was plenty for them to do in fulfilling their special roles without infringing upon the private practitioner. Indeed, if they did their jobs well they would assist and support the private doctor. They would supplement, not replace or compete with, existing medical services.

Within a few years, Mr. Keller had become director of manufacturing for the then new Chrysler Corporation and had the opportunity to put into practice some of the ideas that he and his medical friend had talked about. Mr. Keller was instrumental in establishing a full-time medical staff at Chrysler and later, as president of the company, he was responsible in large measure for many of the actions that made the corporation one of the pioneers in the development of occupational medicine.

and the Manufacturer

L. L. Colbert.

So much has occurred since those days in protecting and maintaining the health of the automobile worker that we often overlook the fact that most of the advances had their beginnings in conversations between physician and manufacturer, such as those between K. T. Keller and his doctor friend three decades ago. Starting with a common concern for the well-being of the people who work in the automobile plants, the doctor and the manager have found that the occupational curiosity of one stimulates the imagination of the other. When they put their minds to work together, things happen that enrich not only them but the community in which they both live and work.

Neither doctor nor manager, for example, could be long satisfied merely with supplying emergency assistance to the victims of accidents or to those workers who became moderately ill during a shift. And so it was not long before doctors in the automobile plants were working with engineers and managers to reduce the causes of accidents and to control fumes, dusts, and mists which might endanger the health of the worker. This attack has been so successful that today an automobile worker is less likely to be hurt in an accident at work than at home. Toxic hazards have been discovered, isolated, and brought under control.

A logical additional step in the early-day evolution of inplant medical services was the examination of prospective new employees and the determination of whether they were physically fit to perform satisfactory work in automobile plants. Inevitably, however, doctors soon began to wonder whether the preemployment physical examination could not serve broader purposes than those originally intended.

One of those who thought about this was the late Dr. John J. Prendergast, medical director of Chrysler. Dr. Prendergast got to wondering about the ability of people who had recovered from tuberculosis to perform satisfactory work. With the support of Chrysler management, he embarked in 1938 on a program to make chest x-rays of new employees. He added to his staff an expert on internal medicine and pulmonary diseases, Dr. Marion W. Jocz, and arranged for the assistance of a leading x-ray expert, Dr. Carl C. Birkelo.

During a five-year period, more than 300,000 physical examinations, including chest x-rays, were made by Chrysler doctors. Altogether, more than 3,000 persons were found to have active or inactive pulmonary lesions—many of them being unaware of this until they applied for work in Chrysler plants or reported for a physical examination after an absence from work due to illness.

Out of these studies came a number of conclusions important to the automobile industry and to the medical profession as well. Among them, for example, was the knowledge that em-

ployment of persons with certain types of inactive pulmonary tuberculosis lesions is practicable. As the doctors said in their formal report, "the usual conditions of employment in a highly mechanized industry do not constitute a threat to the health of such persons or to their fellow employees," and "the work record of these persons appears to be as good as that of other groups of physically substandard employees."

The formal results of this program were not published until 1948, but preliminary findings proved of immense value to the automobile industry during World War II. Young, physically fit men were entering the armed forces, and most applicants for employment in the plants were those unsuited for service because of age or because of various physical and other defects. Applying knowledge gained in the tuberculosis study, the doctors found that many people who in the past might have been denied work because of "physical handicap" could perform excellent work if they were assigned to an appropriate job. A man who could not see well close-up would not be suited for an inspector's job, but he might handle a jitney with great expertness. A man who could not do heavy lifting could operate an automatic machine or run a power lift. As Dr. Max Burnell of General Motors has said, automobile industry doctors concluded that "everyone is handicapped for some kind of work."

A number of doubts about employing previously ill people have been resolved by new medical knowledge. A study by Dr. Jocz and associates, for example, produced evidence that most Chrysler employees who suffered heart attacks could return to work after a suitable period of convalescence. Ninety per cent of the employees studied over a period of years were able to return to suitable jobs.

Most employees of this company who suffered heart attacks during this period were in the older age groups, compared with the general plant population. Because of seniority or ability they qualified in most cases for the lighter jobs, and so two-thirds of them were able to return to the work they were doing before their attacks. The other third had to be assigned to jobs involving some restriction of activity, but, since the automobile industry is so highly mechanized, this was not too difficult to do. Dr. Jocz, who succeeded Dr. Prendergast as Chrysler's medical director, reported that the survival rate of Chrysler employees returning to work after heart attacks "compares favorably with that of similar cases elsewhere, and their rehabilitation and performance on the job has been generally satisfactory."

We are much closer today to really "tailoring the man to fit the job" in the automobile industry, and we are gaining more knowledge all the time as a result of collaboration between the doctors and those who operate the factories.

Spectacular things have happened, too, when doctors and engineers have put their minds to work together in solving medical problems. Some years ago the distinguished Detroit surgeon, Dr. James Barron, concluded that in many cases of internal hemorrhage lives were lost primarily because the patient starved. In such cases the patient frequently is unable to take food in the normal manner, and Dr. Barron concluded that feeding by vein was not adequate.

A major step toward supplying sufficient food for such patients was achieved with the development of a thin plastic tube admirably suited for introducing natural foods into the digestive system through the nose. But two big problems remained: getting food in a form fine enough to be put through the tube, and introducing it at a rate at which it best could be assimilated. Dr. Barron mentioned these problems to Dr. Prendergast one day, and Dr. Prendergast suggested that perhaps the engineers at Chrysler Corporation could come up with the solutions.

Automotive engineers for years had been grinding and pulverizing various materials and pumping oil, gasoline, water, and other materials as part of their research and testing of automobile components. To solve the first part of Dr. Barron's problem, the Chrysler engineers suggested use of a colloid mill, such as that used in the cosmetic industry, for pulverizing and liquefying food fine enough to flow through the small plastic tube. Then, employing a principle that had been known to engineers for more than 100 years, they developed a simple, easily cleaned, sturdy, and trouble-free pump for forcing the food through the tube at rates desired by the doctors. The pump was called the Barron pump, and many similar to it are now in use in hospitals.

Similarly, Dr. F. D. Dodrill had an idea for developing an artificial mechanism which would take over the heart's pumping action temporarily while a patient was undergoing heart surgery. He took his problem up with Charles E.

Wilson, then president of General Motors. The engineers at GM went to work, and the result was the Dodrill-GMR mechanical heart, which now has been used successfully in many heart operations.

The doctors at Chrysler call upon the engineers for help in solving many problems—less spectacular, perhaps, than the Barron pump, but of great importance, nevertheless, in helping answer medical questions.

Chrysler doctors, for example, ran a study in cooperation with a medical center and a public health agency to determine whether heart ailments could be detected before attacks occur. In one of these tests they wanted to make use of a ballistocardiograph to detect body movements associated with heart beat. This proved to be difficult, however, because not far from the medical facilities there was a busy street and also a stamping plant. Passage of heavy trucks and the operation of the big stamping machines produced vibrations that interfered with operation of the highly sensitive ballistocardiograph.

The doctors knew that Chrysler engineers had been measuring and studying vibration in automobiles for years. In fact, one of the most elaborate and exact elements of the engineering establishment is a vibration laboratory. Applying knowledge gained in this work, the engineers built a table for the doctors that is practically free of vibration, and the study proceeded.

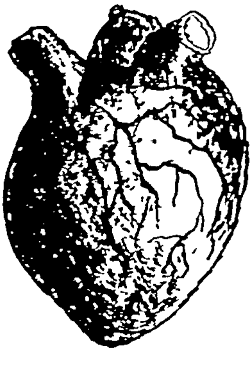
Collaboration between doctor and engineer works both ways. Automotive engineers always have been greatly concerned with building more safety into their products, and they frequently have turned to doctors for information and suggestions involving their problems. Chrysler Corporation and others in the automobile industry currently are supplying funds and cooperating with Cornell University in a program designed to produce new information vital to the industry in further safety advances. In this program, medical societies, state health departments, and state police are working together to compile detailed, specific information about the kinds of injuries sustained in automobile accidents. Many lessons learned already have been applied in such safety devices as padded instrument panels, recessed steering wheel hubs, and safety doorlatches, and there is no doubt that in the months ahead the program will produce much more solid fact on which to base engineering decisions of the future.

We have come a long way since those days when K. T. Keller and his doctor friend discovered their joint concern about the medical care received by industrial workers in the early '20's. Not only do employees today receive prompt and expert medical service if illness occurs during their working day, but much is done to prevent illnesses and to help them secure treatment before serious conditions develop. Industrial doctors consult with the employee, when he requests it, about his health problems or concerns. In many cases, the doctors detect the beginning of conditions which call for careful medical attention and are thus able to urge employees to go to their own physicians for further analysis and treatment.

Close cooperative ties have developed between the industrial and the private physician in many ways. When employees report for a physical examination after an absence due to illness, the industrial doctor frequently confers with the employee's private physician to make sure that the man is assigned to work which his own physician feels he is capable of doing. At the request of private physicians, industrial doctors also serve as consultants in cases where employees are referred to private doctors as a result of preliminary inplant diagnoses.

Doctors in the plants are thus able to supply private physicians with whom they work much information valuable to them in providing the best care for their patients. And the private doctors in return supply the companies with information that is equally important to them in the conduct of their businesses. This kind of creative partnership between doctor and industrialist undoubtedly will continue to grow, producing new and greater benefits for industry, for the medical profession, and for the community at large.

L. L. Colbert
President of the Chrysler Corporation



News Communications

John Daly

Just after the middle of the morning on Tuesday, April 12, 1955, a colleague of mine wen before an American Broadcasting Compan microphone with the following bulletin: "A da of victory—victory over the dread disease infantile paralysis. The official news has just no come from the outposts of the battle line. Th announcement, after comprehensive, protracte scientific survey, is that the Salk polio vaccine 80 to 90% effective in preventing paralytic poli It is 60% effective against type 1 virus and 90 against disease caused by types 2 and 3.

"The vaccine is safe, effective, and potent."

On 3,700 radio stations and 500 television outlets across the United States that memorable midmorning, regular programming was being interrupted, fragmented, thrown out the window, as the words came pouring out of Ann Arbor, Mich. Network stations and big independents took the words directly from their men on the scene; tiny 250-watters in remote communities picked them up from the press association teletypes chattering excitedly.

At 2:30 that afternoon I went on the air to introduce Dr. J. S. Salk himself. In that introduction I said, "This is a day of family rejoicing. Like the happy telling of the smallest details of a christening, a confirmation, a bar mitzvah, a wedding—like the sunny laughter of a cluster of relatives around a young mother's bed." Then Dr. Salk was speaking from Ann Arbor, discussing his victory, describing what had happened in the blood streams of those inoculated children, urging that antipoliomyelitis inoculation become routine.

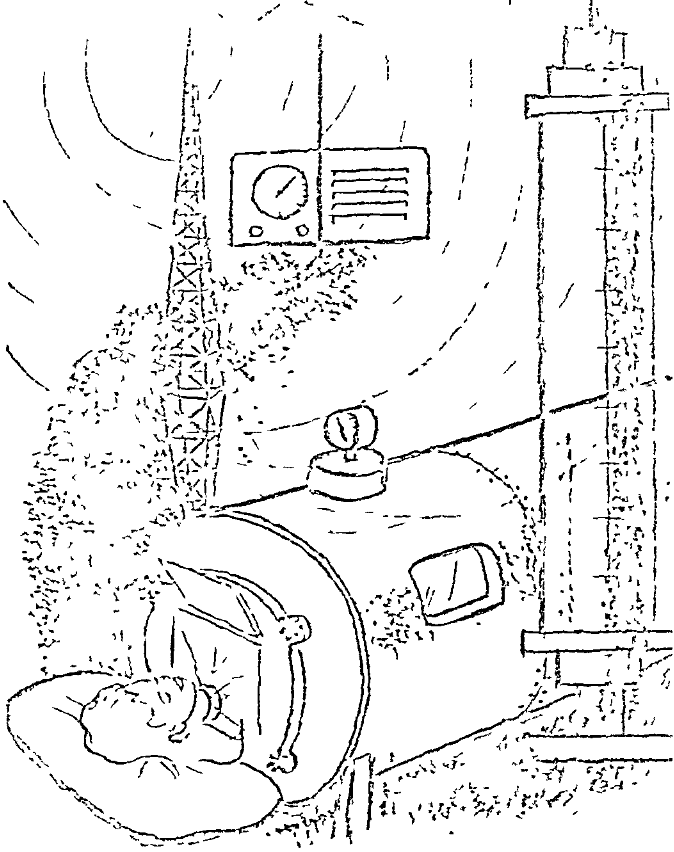
Meanwhile, at the speed of light, which has become our normal operating velocity in this strange, electronic medium, the word had crossed oceans and icecaps and wastelands, racing around the world to meet itself on the other side, diffusing effortlessly even through that most remarkable semipermeable membrane, the Iron Curtain: The vaccine worked.

Then the newspapers, the extra editions, were on the streets of the world with the big headlines and the column after column of side-bar stories—details, statistics, tiebacks, see what the health commissioner has to say, go interview 10 mothers.

"Words, words, words," cries Liza Doolittle. "I'm so sick of words!" But that day the human race couldn't get enough of the words; it hung over the little boxes, pored over the columns of type, picked up the telephone to talk it over with Myrtle down the street.

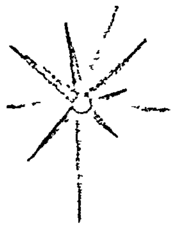
By midnight of April 12, it was a very insulated American, a very insulated human being, who didn't know that medicine had conquered paralytic poliomyelitis.

When I was asked to do this article on news as it is related to medicine, the first thing that crossed my mind was that Tuesday, April 12, 1955. It was, of course, one of the 8 or 10 biggest news days in a century not devoid of big news days, and none of us will ever forget it. But I think that it serves as well to illustrate the three general areas in which the modern news apparatus has become almost an adjunct of modern medicine—an adjunct whose importance neither you nor I tend to realize in the daily round of work.



First, there is the news dissemination itself. Human beings, as you may have noticed, take an intense interest in themselves. Nothing as personal and important to the individual as medicine can fail to have a tremendous impact on the community. The communications business, keyed above all to what is interesting, devotes great portions of its time and space to medicine—only wars, dictators, congressional committees, and the weather claim comparable attention. All newspapers of any consequence carry regular medical columns. So do the major weekly newsmagazines. Every new medical advance of other than the most technical interest is chronicled somewhere in the nation's press, radio, or television.

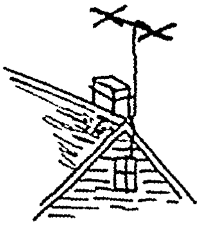
The process can be carried to extremes, of course; I recall the tale of the eminent hypochondriac who rushed into his doctor's office waving the latest edition of a well-known monthly magazine and crying, "Oh, I've got it, doctor, I'm done for." He pointed to an article describing in grisly detail a rare tropical malady, invariably fatal. The most remarkable feature of this ailment, from a medical standpoint, was



that it had absolutely no symptoms. From the onset right through to the end, the patient felt fine, ate heartily, seemed to glow with health.

Flinging his arm tragically across his chest, the hypochondriac moaned, "And that's just how I feel, Doc; oh, save me, save me!"

Yet in its apocryphal way, this little vignette illustrates my point perfectly. It is this vast, continuing lay dissemination of medical developments—spotty though it may be, frequently a headache to you though it may be—which has made attainable the high national health standards of today. I would, in fact, submit that public health as we know it would be a flat impossibility without the modern machinery of news.



The effects of Asian influenza are being kept to a minimum in the United States because when newsmen first heard of the epidemic they went to doctors, asked what people should do about it, and then told the people. One wonders how many of our 170 million or so citizens would have known there was an epidemic, much less what to do about it, if there had been no mass media to tell them.

In 10,000 Chinese village squares, carefully pretuned radios are crying, between Oriental Marxisms, "Swat the fly!" Substandard diets are disappearing because news has reported medicine's work in nutrition ever since thiamin was discovered in 1897. And, to return to my opening illustration, the millions of young people now protected against poliomyelitis are protected because, since April 12, 1955, reporters have been telling them about the vaccine.

We newspeople had a chance to check up on our own effectiveness in the medical area back in 1948, and I think the figures deserve mention here. On April 29, 1948, ABC radio presented a public affairs documentary, accurately titled, "VD: A Conspiracy of Silence." Breaking a major taboo—with, I admit, some trepidation—we did a program frankly aimed at locating infected individuals, persuading them to come to the clinics, and detailing new, highly successful treatment for venereal diseases. Then we ran a survey on our results.

One clinic we spot-checked reported that 25% of the people who came to it in the following weeks learned of it through our broadcast. In one state, 20,000 cases of syphilis were discovered and cured as a result of "VD: A Conspiracy of Silence."

The revolution in the nation's thinking on mental illness can, I think, be credited in great degree to the mass media. A torrent of newspaper, magazine, radio, and television pieces on mental disturbances have brought us, at belated last, to the civilized realization that insanity is an illness, to be regarded, treated, and, increasingly, cured as such.

The point needn't be labored; examples are legion—cancer, alcoholism, heart disease. It could even be argued that, in the complex and highly septic civilization we have evolved today, if there were no such thing as a news industry the medical profession would have to invent it.

Similarly, this continuing coverage has done an enormous public relations job for the medical profession itself. The "Medical Horizons" series took viewers inside dozens of hospitals, even inside operating rooms themselves; it is hoped that the program had the effect of making both doctors and medicine more comprehensible and less fearsome to the audience. All the networks, all the news media, have contributed to this vital understanding.

The second area where I believe news has played a major role in medical work is financial. It was March of Dimes money that supported the Salk experiments, and it was the nation's news media that supported the March of Dimes, with free time and space, with special broadcasts and articles. The United Cerebral Palsy Foundation estimates that in seven years of telethons it has collected between 15 and 25 million dollars for cerebral palsy research. Similar bulky war chests have been raised for multiple sclerosis and muscular dystrophy. It was an old-time newsman named Winchell who originated and now plays mother hen to the burgeoning Damon Runyon Cancer Fund.

It is evident that the skyrocketing cost of broadening medical research has required and will require more and more support from the public at large, with its potentially large volume of individually small contributions. Here too, the news media will continue to play their key role of getting information from where the need is to where the money is.

There is a third field in which my own business, radio and television, is increasingly lending medicine a hand. This is in the matter, surprisingly, of equipment.

I have watched with great interest in my trade journals, as doctors must have in theirs, the startling entry of television into the medical field. Eleven years ago, in February, 1947, a "blue baby" operation was televised for more than 300 physicians and nurses at Johns Hopkins Hospital. Some such technique was even then overdue, what with the ever widening cluster of consultants, specialists, sterile nurses, circulating nurses, and other functionaries obscuring the view of the operating table. Galleries overlooking the operating theaters were fast becoming useless as a means of instruction until the TV camera—the sterile TV camera—came on the scene. But once that ungainly machine rolled into the operating room, the potential audience for an operation became literally limitless—and each viewer watched from just a few inches above the incision.

Since that Johns Hopkins experiment, two even more striking developments, one in technique and one in application, have grown out of operating-room television. Color video made its first medical appearance in 1949, years before it became available to the general public. And color TV in turn led to a procedure which may strike doctors now as commonplace but which still utterly amazes me. On Jan. 19, 1955, an operation in Philadelphia was transmitted via color television to more than 150 doctors at sets in Baltimore and Washington. A magnified image of a tissue specimen, removed within the instant, was shown on the screens, and a Baltimore pathologist gave his diagnosis. The observers in all three cities discussed his finding and confirmed it, and the operation was completed on the basis of their historic examination. One doctor said, correctly I think, "It was like bringing 150 specialists right into the operating room."

This operating-room use of television is the one that really catches the nonprofessional imagination, but it certainly doesn't begin to exhaust the possibilities—or even the actualities. Ultraviolet-sensitive TV is being used in cancer research for comparison studies between normal and malignant tissue. There is talk of using closed-circuit video to supervise entire hospital wards (yes, I think so too, but let's leave Big Brother out of the discussion for the moment).

One rather heart-warming application of medical TV crops up in the Morristown, N. J., hospital, where children too young to be admitted on the wards can "visit" with confined parents over a special video rig.

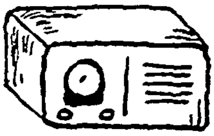
Dr. DeForest's remarkable electron tube itself has proved almost as much a boon to doctors as it has to us newsmen—and it's supporting a great many of us. Consider the electron microscope, x-ray systems, the television microscope, and a whole laboratory full of such measuring devices as the radiation meter and the electrocardiograph. Certainly the world of the future is an electronic one, and we're happy to have you aboard this speedy little particle of ours.

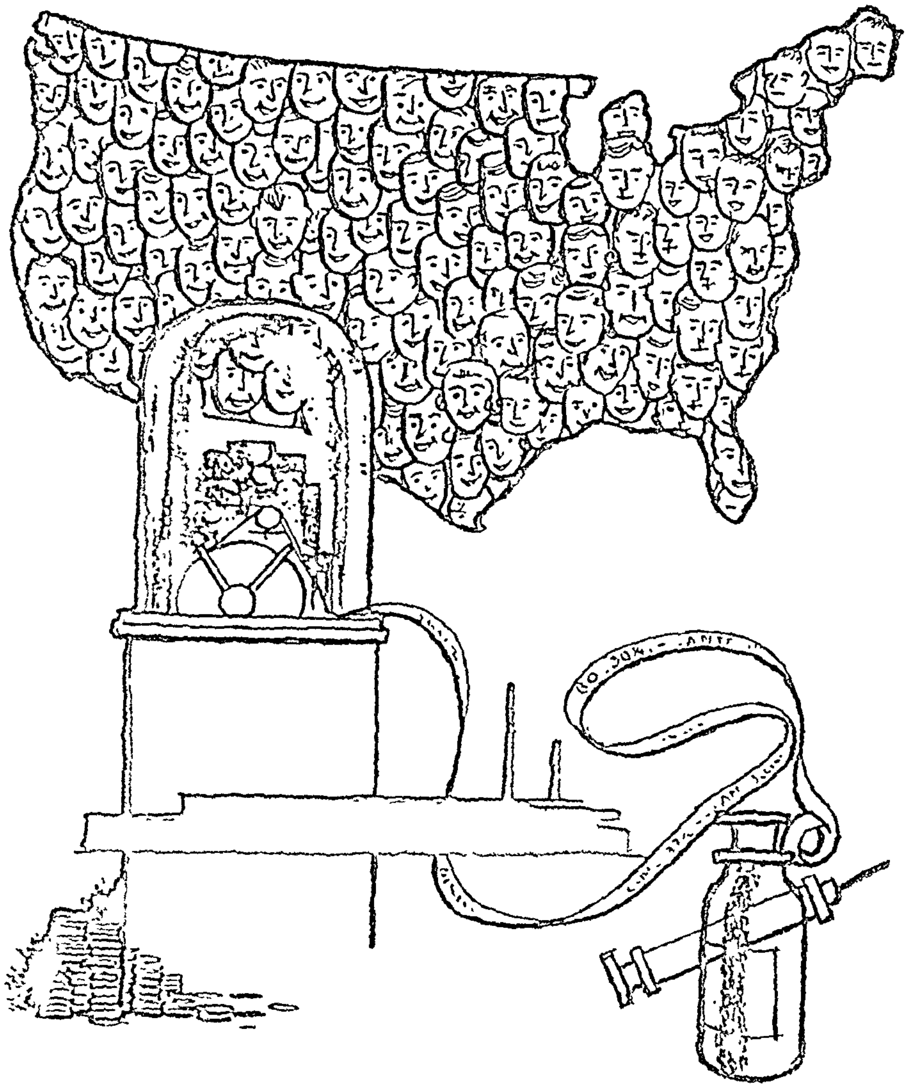
Now, I was asked to write a piece on the benefits that news confers on the world of medicine. I cannot end, however, without fervently thanking the medical profession for the one triumph without which the news business as I know it could not exist. Newsmen, of course, have trekked into the most toxic jungles with impunity, shot full of quinacrine (Atabrine). We've wriggled casually across the rusted barbed wire of a hundred war fronts, our blood streams aswarm with invincible tetanus antibodies. We've talked our way through fire, flood, invasion, whatever the Four Horsemen could throw at us, protected only by a press card, an assured manner, and the miracles of modern medicine. But none of this is what I'm talking about.

The triumph I refer to is a miracle drug in the finest sense of the phrase. On its timely appearance in 1899 the entire towering structure of news today depends. Without it the news fraternity would long since have distributed itself in about equal numbers among the less expensive sanitariums, the foreign legion, and the grave.

I mean, of course, aspirin.

John Daly, Vice-President in charge of
News, Special Events, Sports, and Public Affairs,
American Broadcasting Company





Business and Economics

James E. Day

It seems particularly appropriate that I be asked to contribute an article on the 75th anniversary of THE JOURNAL, inasmuch as the Midwest Stock Exchange has just completed a similar celebration. The doors of the Chicago Stock Exchange, a forerunner of Midwest, were first opened on March 21, 1882. As a result, the year 1957 was our diamond anniversary.

Although in entirely different fields, I think the medical profession and the investment business have much in common. Neither activity enjoyed or merited public acceptance until it raised its own standards and saw to it that they were applied uniformly.

The readers of THE JOURNAL are well aware of the Flexner report in 1910 and how it brought order to medical schools and ultimately to the medical profession. For a good many years now, the securities business has similarly had the confidence of the American people, largely because the development of organized markets and orderly market procedures has convinced the public that anyone can buy or sell his securities with assurance.

Although the handling of securities for customers does not require a degree from an accredited school, as is true in medicine, our people must pass a creditable examination and be registered in the state in which they are located.

One of the most significant historical sites in the country is located not too far from my original home in Cuba, Ill. I am referring to New Salem, the restored village where Abraham Lincoln lived and worked from 1831 to 1837. It does indeed provide a picture of considerable economic importance. It also is a key point of departure for medicine.

There are countless examples of the intelligence and ingenuity of the people who lived in New Salem and elsewhere throughout the world in 1837. In the medical field, brilliant men and women had already discovered or developed vaccine, chloroform, food preservation, the stethoscope, and the thermometer. In business, men had successfully solved many major production and transportation problems by the invention of the cotton gin, the steam engine, the harvester, the locomotive, the plow, and the sewing machine, to name only a few.

Yet even the most casual visitor to New Salem, it seems to me, cannot help but be impressed by the distance we in the United States, as a nation, have traveled in the 125 years since that era. Certainly it was not lack of brainpower that made the civilization of New Salem in 1837 appear so primitive. Instead, I submit that it was lack of materials. The creativity was there, but we were deficient in the tools. (And let me say parenthetically that civilization in 1958 will appear in a very large measure deficient on many fronts when it is spotlighted in 2058.)

What I want to communicate to readers is that human needs are many, numerous, and pressing but that they will not be met until enough capital is accumulated and earmarked to permit the creation, development, advancement, and exploitation of new products or services.

There are countless examples to demonstrate this. If any reader has had time or inclination for what might be termed "casual reading," I'm sure he or she will recognize the importance to the expansion of the economy of such major developments as the automobile, airplane, radio, television, advertising, the telephone, construction, food stores, department stores, and various means of transportation. All of these successes were adequately capitalized eventually.

It has often been said that America, as we know it today, has been built on the skeletons of early failures. Certainly this has been true in the automobile industry. Pause a moment to consider the economic significance of the following startling fact. There have been over 2,000 makes of automobiles on the American market since the motor car was invented less than 70 years ago. Yet today there are only about a dozen remaining!

What happened to the remainder? They all lost their identities as a result of merger, purchase, consolidation, or going out of business. Many reasons are cited for this failure to survive. It is safe to say, however, that most of them can be attributed to lack of adequate capital. In many cases, this took the form of insufficient staying power while knotty production and distribution problems were being solved.

Very much the same pattern of growth and development took place while the radio industry was getting on its feet—and, later on, the television industry. Companies rose and fell as pioneering businessmen formed organizations to produce and market sets. In both industries, every successful company now established is, without exception, one that has been conservatively capitalized.

This matter of capital is the key to the entire economy of the United States. There are many needs yet to be met, but until we have available the kind of capital in sufficient quantities to "get the show on the road," so to speak, the answers to these needs will not be developed.

Right at this moment, more than 2 million patents have been granted by the U. S. Patent Office, but only a small fraction of these are actually produced commercially. Why? Those who have capital have not yet been convinced that they should be financial backers of the entire process of getting these products from the drawing boards to the general public.

Consider for a moment, if you will, the problem of adequate water supply in the United States. Practically every authority in the country who has spoken out on the subject is in agreement that the problem is a serious—perhaps even a critical—one. The water tables are at their lowest levels in many years, and apparently water requirements are so insatiable that the tables are not likely to be restored by natural means alone. Furthermore, the national consumption of water is rising so fast that the U. S. Department of Commerce estimates that, by 1975, daily use will be up to 453 billion gallons, a 73% increase over 1955.

What is being done to alleviate this situation? Well, for one thing, efforts are being made to conserve water—reductions in leakage, reuse of water, treating contaminated water, and other steps. But the logical and most obvious thing to do is to convert sea water to fresh.

This process has been known for many years. The U. S. Navy has developed equipment for emergency use which can convert salt water into fresh. But the operation is far too expensive at this stage to use universally.

One or two companies are now turning out daily batches of converted sea water, but again the cost is very high. These companies are staking their own capital on the chance that they will be leaders when this relatively new industry really gets going. It will eventually, of course, but the path to success will continue to be rough for a long time to come.

Yet some of the fortunes which will be in existence in 10 to 20 years will be the result of shrewd, far-sighted investments made now in companies which will provide materials and equipment to the water conversion industry. This will be the lot of the capitalist, undoubtedly.

Closer to the field of medicine are the drug companies. Although a number of drugs in use today, such as morphine and digitalis, were known at the time THE JOURNAL was launched in 1883, it is my understanding that concerted advances in drug development did not come about until companies willing to base their products in extensive research were organized. Hundreds of millions of dollars risked by leading drug companies have resulted in recent years in the sulfonamides, antihistamines, hormones, and penicillin. In the last 50 years, thanks to new discoveries in many specific areas, 21 years have been added to the life span of the average American. Most of this, of course, has been due to a reduction in infant mortality, but substantial credit is also given to superior medication for people of all ages.

What has been the influence of these developments on American business? More consumers for all goods and services have resulted, and there will be even more to come. (The population, now close to 175 million, is growing at a rate of 3 million people a year.)

One last illustration comes from probably the most exciting field that lies ahead of us today. Current meetings of scientists all over the country are beginning to receive factual progress reports on the peace-time uses of atomic energy. Several hundred millions of dollars are being conserved annually because industry now has available radioactive substances for use in creating new products, improving old ones, and making possible more precise measurement and manufacturing processes. But the companies basing some or much of their operations on the development of atomic energy for their own use found that this phase of their activities is usually a losing proposition.

A leading atomic consultant is an authority for the statement that companies using atomic energy which have not had to put too much into research were, all told, probably as much as 400 to 500 million dollars ahead in profits in 1957. By 1960, this figure might be as high as one billion dollars. But the road has been pretty rocky for those entering the power field. The Atomic Energy Commission recently stated, "Some readjustment was going on in that part of the atomic energy industry concerned with civilian power reactors. Some firms dropped out or reduced their undertakings."

So far, relatively little return has been the rule for stockholders who have sought to put their capital to work in the field of atomic energy. But if those now in the field are joined by others willing to risk capital, the rewards will eventually be tremendous.

Basically, then, the pace and degree of growth and development in the economy of the United States is determined by the amount and kind of capital available. As I have attempted to demonstrate earlier, the opportunities are enormous for risk capital and the returns can be handsome.

There are also many opportunities for income capital, where dividends can be substantial with relative safety of principal. Many highly successful companies, soundly established in their fields, are continually on the lookout for additional funds to obtain new plant and equipment or to market new products. These companies often have long records of consistent dividend payments and offer additional shares to the public as a natural result of their need for expansion.

Where does the capital come from? Fundamentally, it is the excess of what we produce or have the capacity to produce over what we consume. We can obtain capital from the extra we have already accumulated or we can mortgage our future output by obtaining capital on credit. But, over the long run, it must rise out of production.

That democratic nation is soundest that has the greatest percentage of its citizens solvent, employed, and comfortably situated. And it is from these people, for the most part, that the capital will stem which will serve as a base for further expansion. It is the primary function of the securities business to bring this about.

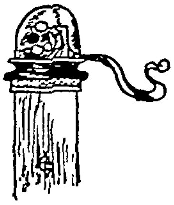
At the Midwest Stock Exchange, a great ground swell of interest in the fundamentals of investing on the part of the general public has been witnessed. Recent surveys have indicated that the number of public stockholders of American corporations has been increasing by leaps and bounds since World War II. There are now close to 10 million stockholders, or approximately 1 out of every 10 adults.

There will be more, as individuals recognize that they can help to protect themselves against inflationary forces in the economic cycle by investing their surplus funds wisely in sound common stocks. Those who can afford to do so may consider their funds risk capital and thereby seek the returns this kind of endorsement may bring.

Thirty years ago, 70% or more of the total stock market volume in the country originated with professional traders on the nation's exchanges. This meant that the public was responsible for less than 30% of the volume. Today, the nation's organized exchanges are truly public market places, since more than 85% of the volume arises out of the transactions of individuals. This is a record of which all those engaged in the securities business are proud.

Although we are all keenly conscious of our shortcomings as a nation, I'm a great one for counting my blessings. I can't help feeling pride in the growth and progress the United States has recorded in the last 75 years in such fields as transportation, education, construction, religion, health, and medicine. Perhaps those in other fields believe that the record of business and finance is noteworthy as well.

James E. Day
President of the Midwest Stock Exchange



Film Entertainment and Community Life

Walt Disney

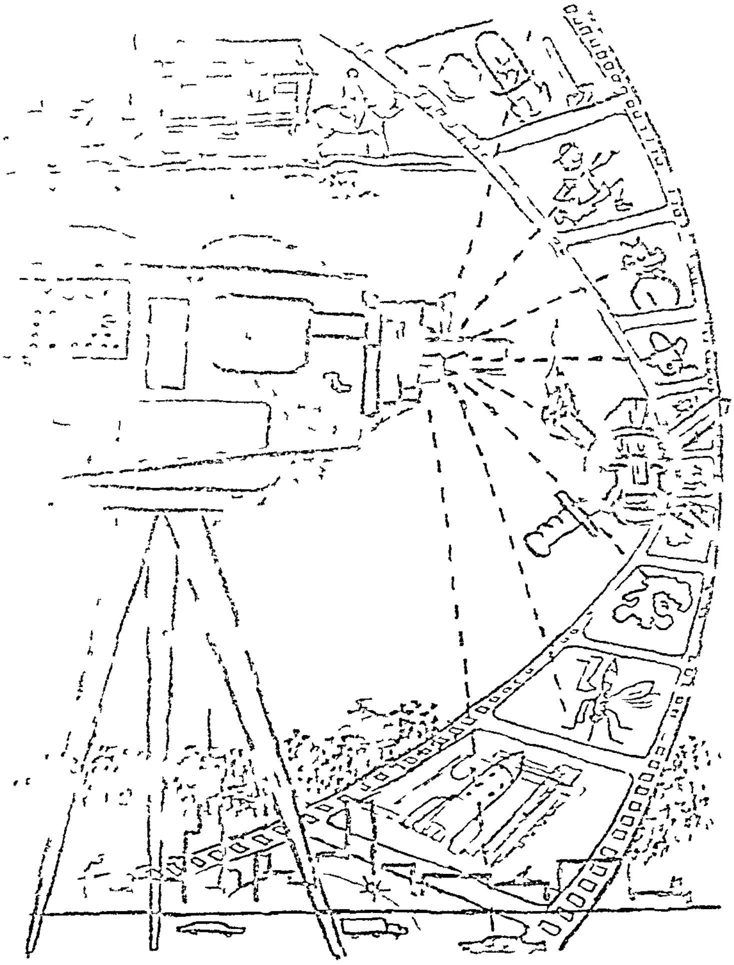
In behalf of our branch of show business, may I respectfully offer congratulations to the American Medical Association on the 75th Anniversary of THE JOURNAL for its fine contribution to the national welfare.

The motion picture industry feels a particularly close kinship with the medical profession in that we too seek to serve the country's well-being.

We do it with prescriptions for pleasure. Mass entertainment, we believe, is a vital public necessity—as important as food, shelter, and a job. The tonic effect of fun and play has long been recognized as an antidote to the stresses, worries, labors, and responsibilities of our workaday life.

The history of our days from nickelodeon to the verge of the space age is considerably less than the A. M. A.'s life span. My own experiences in Hollywood go back 35 years. During that time I have watched the motion picture develop from a mystifying trick—an amusing plaything first known as "the flickers"—to a great art-craft showing daily in thousands of theaters in every city and hamlet in the United States and in thousands more abroad.

In some degree it has conditioned the lives of countless millions around the globe. It has set



styles of behavior, standards of beauty, romantic ideals, and admirable goals of aspiration. Mechanically, the motion picture has become one of the marvels of all time, a true Wonder of the World in its magical powers. But what it has wrought on the screen for every man and his family to see and ponder has been even more wonderful.

In its progression during the past few decades, the film industry has, in a way, paralleled the pattern of medical practice during the same period. Just as circumstances forced the successor of the venerable country doctor from his house calls to the cities with their hospitals and clinics, so the pioneer showman with his small theater on Main Street had to give way to the big-time operators with their plush palaces of the new Rialtos, the Roxies, the Music Halls, the Pantages, the Chinese, where masses of people could be accommodated. The flickers became respectable. They no longer relied merely on amazement. They were being accepted as a people's theater and a popular art.

Dedicated to Laughter

In its early heyday the motion picture screen was mainly dedicated to comedy—broad slapstick which everyone could recognize as true American humor. It derived mainly from the school of newspaper comic cartoons and strips. Here and there it had shadings of satirical mockery, poking fun in good democratic freedom at men and things.

This was the era of the great comics bred to the cinema—Chaplin, Lloyd, Keaton, the Mack Sennett jesters, and others whose like are seen no more. In those days "entertainment" was bounded and defined by the number of laughs it could garner.

But soon, in its swift expansion, the screen added more dignified material to the slapstick and pathetic buffoonery. While the kings of comedy still held their place, the movies adopted "culture." Players were recruited from the stage. Popular authors were hired to adapt their own books and the old classics. This in turn brought on a great increase in book reading and presold audiences. Attendance at film theaters skyrocketed.

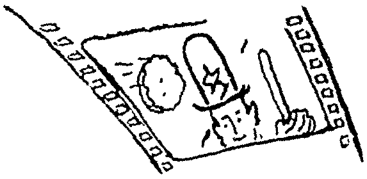
Glorification of Personalities

The star system, with its fabulous paychecks, came into full flower. Glamorous female personalities were "discovered" by studio heads and acclaimed as queens. Their glorification rose to incredible degree. Fan clubs swarmed. Favorites were hysterically mobbed. These were the early ways in which the most remarkable impact in the whole history of mass entertainment began to take hold of American families.

Advances in technology added color, sound (in 1928), and other dimensions to the enchantments of the cinematic arts. It was these mechanical items—sometimes called "magical"—which were of particular interest to my own producing company. We were engaged—and had been since my arrival in Hollywood in 1923—in making fantasies and fairytales which could be done only in cartoon animation. We, too, had contributed to the star system with the antics of a little fellow named Mickey Mouse. Techniques of photography and sound recording were of great interest to us. And our own camera experts and sound engineers have to this day never ceased in their efforts to improve the mechanics of the medium.

Film cycles have run fast, merging, overlapping. Each has to some extent reflected its times in human affairs and temper. In these cycles and themes the historical pageant of the films records its brief half century of existence.

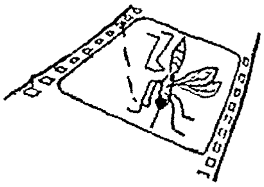
There were the early clownings, the short comedies, the first attempts at telling a story, in one reel, merely to show the amazing facility of the picture-in-motion. Then more elaborate and pretentious two-reelers and longer features.



The suspenseful cliff-hanger serials. Dashing westerns—gun noisy, after the advent of sound. Rustic drama. Sentimental romantics—some simple, some "sophisticated." Historical pageants with their pomps and hordes of extras. The hard, shocking, battlefield realism of World War I. Flaming youth. The violence of the gangster era. The whodunits. Message pictures and topicals, covering more and more territory of American life. Musicals and escapist stuff. And, if I may be permitted—"Snow White and the Seven Dwarfs," to mark a new era in cartoon animation as the first full feature in this medium.

A Business and an Art

The recital of fashions in product from the early 1900's to the present day needs explanation. To comprehend our place and problems, the industry must be understood as a business—the business of wholesaling the merchandise of visual delights to millions. After our first astounding experiences as individual showmen, we began to realize that our community of influence embraced the whole population, not just a local segment. We had to be all things to all men.



As an "industry" we were a lot of competing private enterprisers showing our offerings to the same audiences. A common product poured from the Hollywood studios annually in hundreds of short subjects and features. Motion pictures became a fixed habit of some 80 million Americans in some 20,000 theaters every week.

As patronage swelled to incredible figures, every neighborhood had its local theater and family attendance. Showmen who exhibited our product identified themselves with other groups and institutions of vital importance to the locality in the name of the whole industry.

One personal experience in close relationship with other major groups—in this case the medical profession and the public health service—occurred during World War II, when we were happily able to make films useful in fighting disease and the ignorance which has tolerated it. Distribution was through the Coordinator of Inter-American Affairs. These film educationals included methods to control malaria, dealt with precautions against polluted water, illustrated the attack of science on germ infection. Environmental sanitation, eating for good health, a definition of disease, and the functions of the human body were other areas of concern. They applied to our servicemen abroad and to certain South American and Central American populations.

The Challenge of the Space Age

Today we stand at the threshold of the space age. Now, once more, we must attempt to diagnose mass taste and preference in what may well be the most critical era for motion pictures. We must diagnose and prepare the prescription.

About one thing I feel certain. Tomorrow's show world will have to be more aware of our physical environment. Fascinating fact will vie with the most beguiling fantasy. Teen-aged seekers of diversion and those steeped in the sciences especially will expect a much broader definition of what the trade has always called "entertainment." The theater will have to compete with all the excitements and fascinations which science education will add to the humanities in real life.

Escapist fiction will have two channels—one into the past, another into the future. Enlightenment will be a staple alongside of amusement. We already have evidence of this in our own studio in the growing audience reception of our True-Life nature fact films and such science speculatives as "Man in Space," "Man and the Moon," "Mars and Beyond."

"Science Will Never Destroy Myth"

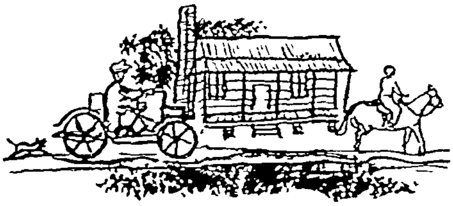
I do not mean to disparage the best in human drama, in myth and timeless fairytale, in stirring legend and heroic adventure. These will never be diminished. The human spirit needs them in every age. Spiritual health requires them. But our film programs, in theaters and on television, will unquestionably demand more balance, more discrimination, wider appeal and a broader common denominator.

Our own schedule for the next few years ahead will confidently complement a "Sleeping Beauty" and other sheer cartoon fantasies with more true wildlife dramas, factual reports of people and places, and live action human drama tied in with the newly disclosed marvels of the atomic and electronic age.

I believe implicitly that the motion picture still has great things ahead. Equipped with its big screens, its color and sound fidelities, and all its perfected devices for illusionment, nothing is beyond its range and powers.

Itself a marvel of science, it can and will serve with equal facility the space enthusiast looking beyond the sun and the homebody content with the warm familiar earth and all its bounties when he goes with his family seeking entertainment and inspiration.

Walt Disney
Executive Producer and Chairman
of the Board of Walt Disney Productions



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Chicago Letter.—Rush Medical College is about to build a hospital of its own on ground in close proximity to the college buildings. The hospital will be built so that it can be enlarged in the future. The college is undoubtedly led to make this move because of the many hinderances thrown in the way of clinical teaching in the County Hospital, by the County Commissioners. During the last two years or more, the students have not been allowed to enter the wards, and go to the bedside for instruction, but have been required to receive all clinical instruction in the amphitheater. . . . The New St. Luke's Hospital is fast nearing completion, and will be ready for occupancy in the course of a few months. This hospital has long needed enlargement. Its wards are always full to overflowing. The new building is expected to be one of the best planned hospitals in the country. They still have as much more ground as is now used, on which they can build in the future. This hospital will furnish much additional clinical material for the students of the Chicago Medical College. The hospital is only a few blocks from the college, and three of its staff are professors in that institution. The Chicago Medical College is now peculiarly well supplied with clinical material, for in addition to St. Luke's Hospital, it still has the use of the material in Mercy Hospital . . . on the same grounds with the college. Mercy Hospital accommodates between two and three hundred patients. Some four or five blocks off there is also the Michael Reese Hospital, in which occasional private clinics are held.—Correspondence, THE JOURNAL, vol. 1, July 28, 1883, page 90.

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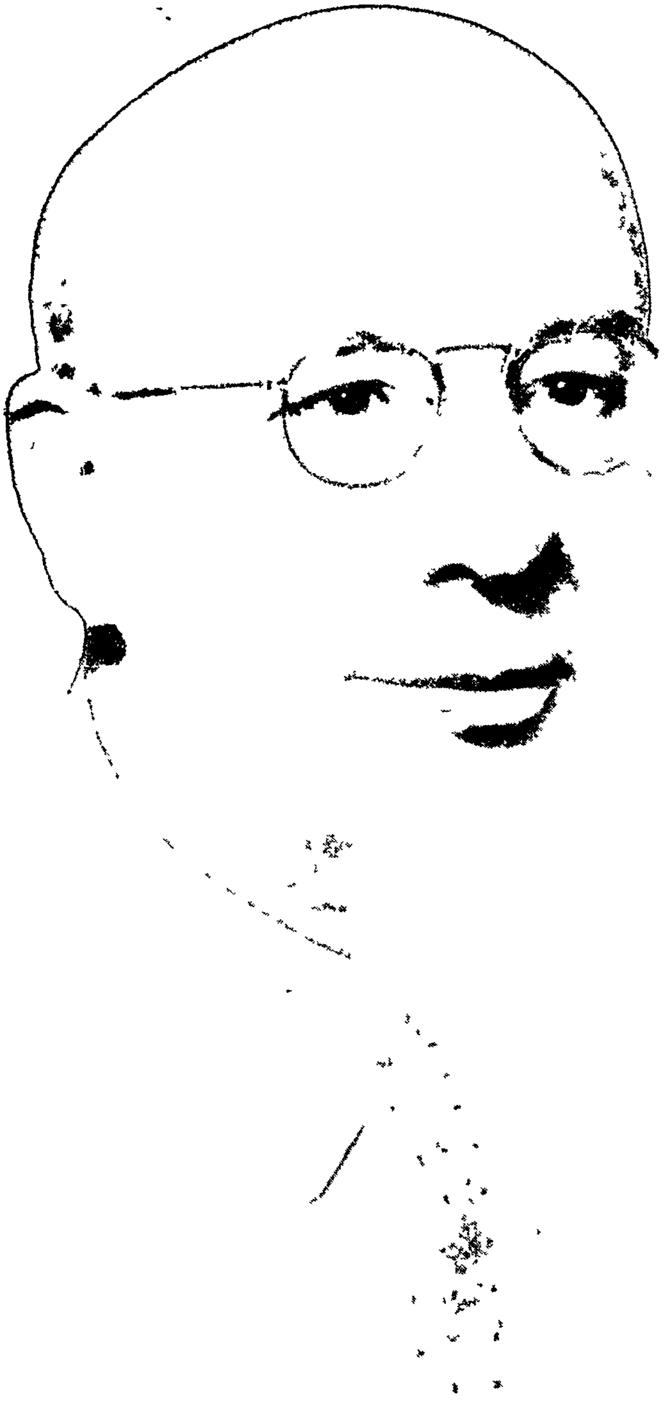

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ANTIGENIC PECULIARITIES OF 1957 INFLUENZA VIRUSES AND SEROLOGIC INDEXES OF IMMUNITY AMONG THE POPULATION

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This investigation was undertaken to determine whether the peculiarities of circulating influenza viruses and the state of anti-influenzal immunity of the population might have contributed to the spread of the influenza pandemic of 1957. Strains of influenza virus isolated during June and July in and about Moscow were used. The antigenic patterns of 15 Russian strains are tabulated and compared with two different Singapore 1957 strains obtained by way of England and the United States. Despite the complexity of these patterns, some classification was possible. The hemagglutination tests must be supplemented by other serologic tests in the study of serologic shifts with respect to new strains. The neutralization test in particular was found to be sensitive and informative, since it detected antibodies against certain strains in serums which had no antihemagglutinins for these strains. The most extensive outbreaks of the disease occurred in cities where the titers of antihemagglutinins among the population were the lowest. The assembled data show that changes occurred in the immunity of the population as well as in the characteristics of the viruses as the pandemic developed.

The pandemic wave of influenza which spread over the globe in 1957 has again attracted the attention of investigators to this disease. Study of this pandemic has brought to the fore new peculiarities in the spread of the disease. On the one hand was the high contagiousness of the disease in "flu areas," where most of the people in large collectives and populated areas became ill with influenza. On the other hand was the fact that some areas were free from the disease during the first six months of the pandemic.

This may perhaps be accounted for by the fact that the pandemic wave spread during the summertime, i. e., a period of the year that is not conducive to the dissemination of the disease, although peculiarities of the circulating viruses and the state of anti-influenzal immunity in the population may also have been contributing factors.

It was to check on this last assumption that the present investigation was undertaken, and the preliminary results are presented in this communication.

Materials and Methods

Viruses.—The strains of influenza virus isolated during June-July, 1957, in Moscow and surrounding area were used for the investigation. The viruses were used in the form of allantoic fluid after four to eight passages in embryonated chicken eggs.

From the Institute of Virology, Academy of Medical Sciences.

Antiserums.—To determine the antigenic pattern of the viruses we used the serums of rats immunized with prototype strains of influenza virus types A, A′, B, C, and D and also strains isolated in 1957.

Rats weighing 150-200 Gm. received two intraperitoneal injections of 2 ml. of undiluted allantoic fluid, containing live virus, at an interval of seven days. They were bled 10 to 12 days after the second injection. In view of the feeble antigenicity of the new influenza strains, the cycle of two injections was repeated after an interval of one month. The strains used for these investigations were A-PR 8, A-Shklaver, A′-Pan, B-Kri, C-Moscow, and D-Moscow and also newly isolated influenza virus strains.

Samples of human serum taken from donors throughout the Soviet Union in 1956 and 1957 were also studied. To remove nonspecific inhibitors, the serums were processed with carbon dioxide by the method of Fridman[1] and Gorbunova.[2] Serums diluted 1:10 with distilled water were saturated with carbon dioxide until a stable precipitate formed. The centrifuged supernatant fluid was used for the tests.

Serologic Reactions.—Hemagglutination-inhibition tests and neutralization in tissue culture were used. The hemagglutination-inhibition test was conducted by the commonly used method,[3] with the chicken erythrocytes. Virus neutralization tests were carried out in cultures consisting of small pieces of chorioallantoic membrane of chick embryos and nutrient medium in glass tubes. Fulton and Armitage,[4] Tamm, Folkers, and Horsfall,[5] and Ryabova[6] successfully used this method for the selection of substances possessing virostatic activity. We used undiluted serum and varying dilutions of virus, and the neutralization index represents the ratio of the titer of virus in the control and serum mixtures. The controls were virus without serum and virus with normal (nonimmune) serum. All serums were heated at 56 C for 30 minutes before being used in the experiments described below.

Antigenic Pattern of Influenza Viruses Isolated in 1957 and Selection of Strains for Study

In June and July of 1957 we isolated 20 strains of influenza virus from patients with clinical influenza. The results of an analysis of their antigenic constitution by means of hemagglutination-inhibition tests are shown in table 1. It is clear that the antigenic pattern of the 1957 influenza strains differed considerably from the previously known viruses, thus forming an independent serologic group. Two subgroups can be differentiated among the 1957 strains.

TABLE 1.—*Analysis of Antigenic Pattern of Influenza-Virus Strains Isolated in 1957 by Hemagglutination-Inhibition*

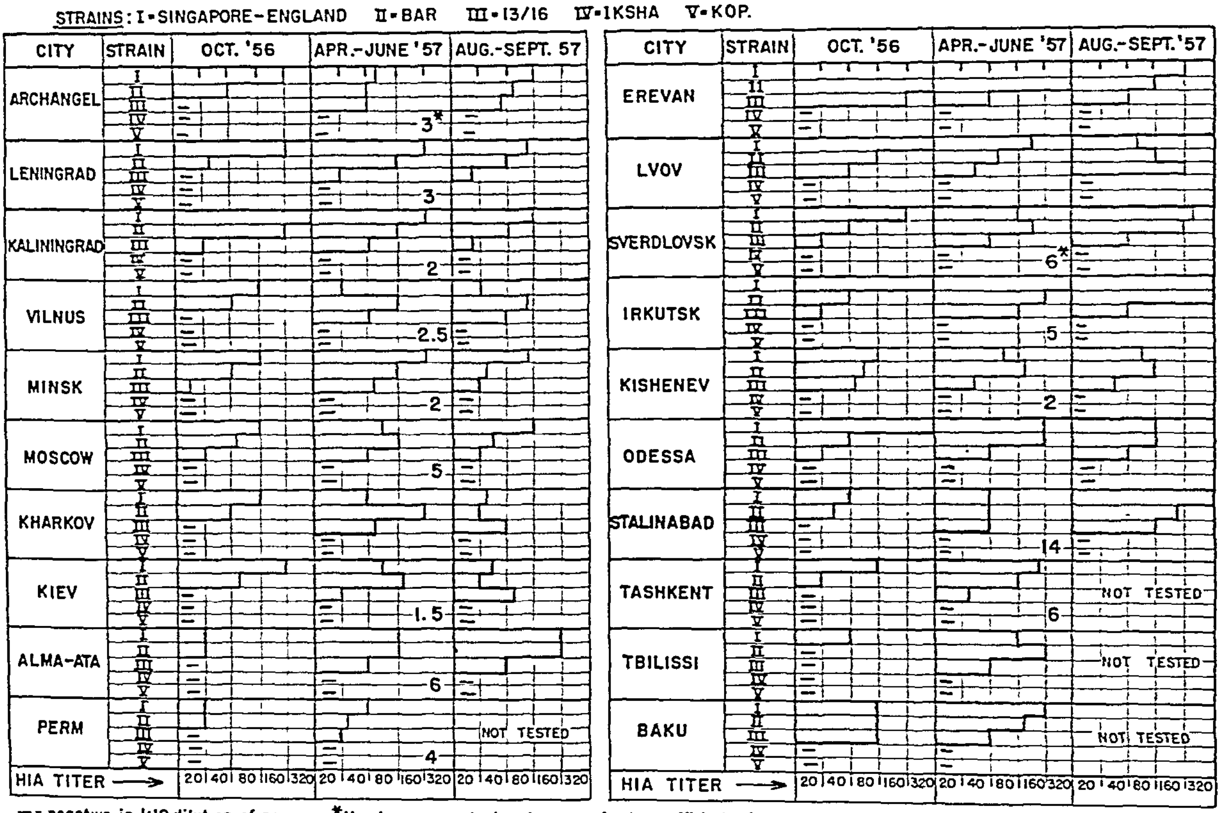
	Rat Antiserums Prepared with*																
	Standard Strains						1957 Strains										
Viruses	A-PR 8	A-Shklaver	A′-Pan	B-Kri	C-Moscow	D-Moscow	Singapore (England)	Bar	49	72	KSK	65	80	66	Kop	34	Singapore (U.S.A.)
A-PR 8	1	⅛	1/16	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Shklaver	1/16	1	1/32	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A′-Pan	1/32	1/32	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Kri	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
C-Moscow	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
D-Moscow	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Singapore (England)	1/16	0	0	0	0	0	1	1	1	½	1	8	4	4	4	8	4
Bar	1/32	0	0	0	0	0	1	1	1	1	½	8	4	4	4	4	4
49	0	0	0	0	0	0	½	¾	1	1	½	8	4	2	8	4	2
72	0	0	0	0	0	0	½	½	1	1	¾	8	2	4	4	8	4
KSK	1/32	1/32	1/32	0	0	0	1	1	1	½	1	2	1	1	4	4	2
65	0	0	0	0	0	0	¼	½	¼	¼	¼	1	1	1	1	2	1
80	0	0	0	0	0	0	½	¼	¼	¼	¼	1	1	2	1	1	1
66	0	0	0	0	0	0	½	½	¼	½	¼	1	2	1	0	0	0
Kop	0	0	0	0	0	0	¼	¼	⅛	⅛	¼	½	½	½	1	1	¾
34	0	0	0	0	0	0	¼	¼	¼	¼	¼	½	1	½	½	1	¼
Singapore (U.S.A.)	0	0	0	0	0	0	¼	¼	¼	¼	¼	½	½	½	½	1	1
Titer of serum with homologous virus	320	320	320	320	160	160	160	320	320	320	160	40	40	40	80	40	40

* Fractions express the relation of the homologous titer of the antiserum to the heterologous one; 0 indicates the ratio is below 1/64 or the virus did not react with a given serum; units and integers show that a given virus is inhibited by heterologous serum in titers equal to or larger than the corresponding homologous virus.

The first subgroup of strains (Bar, 49, 72, KSK, and the strain Singapore/57 obtained from England) reacts actively with homologous and heterologous serums (avid strains). The second subgroup of strains (66, Kop, 34, and the strain Singapore/57 obtained from the U. S. A.) reacts less actively with homologous than with heterologous serums and is not completely inhibited by the serums of the first subgroup (nonavid strains). There is an intermediate group of strains too (65, 80, and maybe 66).

Supplementary investigations which were carried out showed that the strains of the avid and nonavid groups have some further properties which

Thus, the avid variants were highly sensitive to inhibitors present in normal serums of horse, rabbit, rooster, rat, and other animals. Only mouse serums were without activity against the strains of both subgroups. At the same time avid strains did not agglutinate erythrocytes of the mouse and cow, while nonavid strains agglutinate them in relatively high titers (1:80-1:160). Also, some of the strains of the avid subgroup gave polytypic reactions with serums of previously isolated A and A′ viruses. These group (cross) reactions were especially marked with serums which had been stored for more than a year at 4 C, which might be due to incomplete removal of inhibitors present in them.



— = negative in 1:10 dilution of serum. *Numbers in central columns refer to coefficient of increase in incidence of clinical influenza in the population of a given city between April and August, 1957

Concentration of hemagglutination-inhibition antibody (HIA) against new influenza strains (A-57) in pools of serums from health persons in indicated cities of U. S. S. R.

However, even when fresh rat antiserums were used after treating them with carbon dioxide (which in this case completely removes the inhibitors), some of the avid strains (Bar, KSK) still reacted with antiserums of A and A′ strains to 1/16-1/32 of their titer. It is not clear whether these cross-reactions are due to antibodies or to incompletely removed inhibitors.

The following strains have been studied in addition to those isolated in our laboratory: strain "Iksha," which was used for the preparation of a live virus vaccine[7]; strain 13/16, isolated by N. N. Orlova and em[illegible] Virology, Academy of Medical Sciences. anti-influenzal horse serum; and also strains A/Singapore/57 kindly sent to us by Dr. C. H. Andrewes from London and by Dr. J. Smadel from the United States. Strain "Iksha" belonged to the second nonavid subgroup. It is interesting to note that the strains A/Singapore/57 which were received from England and America did not prove to be identical; the English strain belonged to the first subgroup and the American strain to the second subgroup.

Strain 13/16 was isolated from a pool of nasopharyngeal washings of patients during the summer of 1957. It was closely related to previous A viruses and also had some antigenic relation to the 1957 pandemic viruses (1/2-1/16 of titer). It is possible that this virus is a *mixture of two* or more strains.

Studies on Human Serum

Two strains were used for studying the serologic indexes of immunity to influenza in various populations: Bar, representing the first avid subgroup; and Kop, representing the second (nonavid) subgroup. The serums were studied also to determine the level of antibodies to strains A/Singapore/57 (England), 13/16, and "Iksha." Adult human serums obtained at three different periods during

1956-1957 were tested for the presence of antibody against the new strains of influenza virus: (*a*) October, 1956; (*b*) April-June, 1957; and (*c*) the end of August and beginning of September, 1957. Altogether 266 pools of serums taken from 3,990 persons were investigated. Each pool contained serums from 15 individuals.

TABLE 2.—*Some Properties of Avid and Nonavid Strains of Influenza Virus Isolated in 1957*

Strains	Sensitivity to Inhibitors	Agglutination of Mouse and Cow Erythrocytes	Titer Ratio Homologous: Heterologous	Reaction with A and A′ Serums
Avid	+	−	>1	+or−
Nonavid ..	−	+	<1	−

The figure shows the titers of hemagglutination-inhibition antibody against the new strains in the serums obtained from the populations of various cities. It may be seen that antibody for the avid group of 1957 viruses (Singapore, Bar, 13/16) were detected in the serums obtained in 1956, i. e., prior to the appearance of the new viruses, while the same serums did not react with the nonavid group of viruses (Kop, "Iksha").

If one compares the levels of antibody in the serums obtained from the population of various cities in 1956, one will notice that in some of the cities they were rather high, e. g., Kaliningrad, Irkutsk, while in others they were very low, e. g., Alma-Ata, Perm. When one compares the serologic indexes in 1956 with the incidence of the disease in the summer months, it is possible to notice a certain connection. The most extensive outbreaks of the disease occurred in the cities where the titers of antihemagglutinins among the population were the lowest. A considerable rise in the incidence of the disease was also observed, however, in the cities where fairly high titers were detected in the samples of 1956. In some of the cities an increase in the titers of antihemagglutinins to the avid strains was noted in the samples of serums obtained in September, 1957. However, even in the cities where outbreaks of the disease occurred during the summer, the serums obtained during the autumn did not contain anti-hemagglutinins for the nonavid strains.

It must be mentioned that antibodies to the strains 13/16 were absent in serums obtained from many cities in 1956. We believe that some irregular results obtained with the strain 13/16 might be due to the origin and properties of this strain mentioned above.

To test the effect of mixing serums on the titers exhibited by the pools, a number of serums were submitted to parallel study (table 3). As is evident from the table, among the persons examined in September, 1957, only a few had antihemagglutinins to the nonavid strains and the average titer of the serums did not reach the level of the initial dilution of the serum in the hemagglutination-inhibition reaction (1:10). In this connection it is worth mentioning that many persons who had high levels of antihemagglutinins for the avid strains had no demonstrable inhibition for the nonavid strains.

It was of some interest to determine whether the human serums contained no antibodies for the nonavid strains or whether they could not be demonstrated by the hemagglutination-inhibition reaction. The answer could be obtained by using other methods for detecting antibodies, as for instance in the neutralization reaction.

The parallel investigation of several pools of serums by means of the hemagglutination-inhibition and the neutralization reactions indicated that with the avid strains (Singapore, Bar) there was a good correlation between the titers of antihemagglutinins and virus-neutralizing antibodies, but not so with the nonavid (Kop) strain (table 4). The serums, which all gave negative results in the hemagglutination-inhibition reaction with the Kop strain, in some instances also had no significant neutralizing antibodies (0-10), and in others had neutralization indexes of 100 to 1,000,000. Comparing the virus-neutralizing activity of serums obtained at different times, one can see that the average level of antibodies against the avid strains (it relates mainly to the Singapore strain) was approximately the same in the serums obtained in 1956 and in those of 1957.

TABLE 3.—*Comparison of Titers of Hemagglutination-Inhibition Antibodies in Human Serums Tested Separately and in Mixtures*

		Avid Strains			Nonavid Strains	
Mixture	Serum	13/16	Bar	Singapore (England)	Kop	Iksha
I	1	40	20	20	20	0
	2	320	20	10	0	0
	3	80	10	0	0	0
	4	80	80	40	20	20
	5	40	20	10	0	0
	6	40	20	10	0	0
	7	40	40	20	40	20
	8	320	40	20	10	10
	9	80	40	20	0	10
	10	80	40	20	0	0
	Average	118	33	17	7	5
	Titer of mixture	80	40	20	0	0
II	1	40	20	40	0	0
	2	40	80	80	0	0
	3	80	10	160	0	20
	4	80	80	40	20	10
	5	20	160	80	0	10
	6	10	320	80	0	0
	7	20	160	40	0	20
	8	10	0	160	0	0
	9	320	0	320	40	0
	10	80	20	40	0	0
	11	160	40	80	0	10
	Average	74	64	101	5	6
	Titer of mixture	80	80	80	0	0

As regards the nonavid strain (Kop), no virus-neutralizing antibodies were detected in the 1956 series of serums, whereas in the serums obtained after the spring-summer outbreaks of the disease they started to appear, although on the whole their level was much lower than the level of antibodies against the avid strains.

In addition to the pools of serums from healthy individuals, we also studied serums from persons who had influenza or who had received live virus vaccine prepared from the new strains (table 5). In tests with the nonavid strain (Kop) the serums exhibited a rise in titers of the neutralizing antibody, and in 13 of 14 cases there was no demonstrable antibody in the hemagglutination-inhibition test.

Comment

The investigations conducted in our laboratory show that the strains of the influenza virus which caused the pandemic of 1957 not only differ in antigenic pattern from the previously known strains but also form subgroups which differ greatly as regards avidity for antihemagglutinins. Mulder and co-workers[8] established the existence of subgroups of varying avidity for antibody within one serotype. Strains of type A′ isolated in 1949 were subdivided into three groups of different avidity (P, Q, and R). According to this scheme we may classify the new influenza strains as follows: strains Kop, 34, and Singapore (U. S. A.)–Q variants, strains Singapore (England), Bar, and KSK–R variants. Of special interest is the fact that Q variants were completely nonsensitive to the inhibitors in normal rat serum while R variants were partially inhibited by them. The data we obtained in our studies of human serums prior to and after the pandemic wave indicate that these variants may have significance in the development of the epidemic process.

TABLE 4.–*Comparative Titers of Antihemagglutinins and Virus-Neutralizing Antibodies in Pools of Human Serums*

		Avid Strains*				Nonavid Strain*	
		Singapore (England)		Bar		Kop	
Yr	City of Origin of Pools	HI	NI	HI	NI	HI	NI
1956	Tbilisi	0	500	0	10	0	0
1956	Alma Ata	20	10	0	10	0	0
1956	Sverdlovsk	10	1,000	10	1,000	0	0
1956	Leningrad	100	10,000	20	100	0	10
1956	Irkutsk	640	100,000	40	300	0	10
1957	Irkutsk	320	n t	40	10,000	0	1,000,000
1957	Novosibirsk	80	10,000	40	10,000	0	1,000
1957	L'vov	80	100,000	40	1,000,000	0	100
1957	Kiev	n t	n t	40	1,000,000	0	10
1957	Kiev	40	n t	80	1,000,000	0	100

* HI = hemagglutination inhibition test; NI = neutralization index of undiluted serum; n t = not tested

Evidently variation is not confined to antigenic pattern but also is associated with changes in the avidity of the virus for antibodies. It is possible that avid variants which react well with group antibodies represent the first stage of variation in which some relationship to the parent strains is still preserved. Nonavid strains which do not react with group antibodies may represent a further stage in variation of the virus. At this stage not only does the virus completely diverge from its parent as regards antigenic structure but, together with a loss of sensitivity to the action of inhibitors, its capacity for spread is also increased. These nonavid variants can be called, in effect, type A″, because they have no direct relationship with type A and A′, although there is an indirect connection with the latter through the avid variants. This stage of virus variation when nonavid variants appear may be of significance in the development of a pandemic wave of this disease. However, further investigations are necessary to elucidate this phenomenon.

TABLE 5.–*Increase of Antibodies Against Nonavid Kop Strain in the Serums of Patients and Vaccinated Persons*

		Hemagglutination-Inhibition Test		Neutralization Test	
Person No *	Specimen of Serum†	Titer	Coefficient of Increase	Index	Coefficient of Increase
41	I	0		10	
	II	0	0	10,000	1,000
9	I	0		100	
	II	0	0	10,000	100
21	I	0		100	
	II	0	0	10,000	100
23	I	0		10	
	II	0	0	1,000,000	100,000
65	I	0		0	
	II	0	0	100,000	100,000
66	I	0		100	
	II	0	0	1,000,000	10,000
391	I	0		0	
	II	0	0	10,000	10,000
394	I	0		0	
	II	0	0	10,000	10,000
396	I	0		0	
	II	0	0	10,000	10,000
397	I	0		100	
	II	0	0	10,000	100
2 (v)	I	0		<10	
	II	0	0	10,000	10,000
4 (v)	I	0		10	
	II	0	0	1,000	100
7 (v)	I	0		10	
	II	0	0	10,000	1,000
9 (v)	I	20		100	
	II	40	2	10,000	100

* (v) = vaccinated persons, serums taken from vaccinated persons were used in a 1 10 dilution in both tests (HI and NI)

† I = serum taken at the beginning of disease or prior to vaccination; II = serum taken 2 3 wk after serum I

The data we have obtained demonstrate that, in the study of serologic shifts with respect to new strains, the hemagglutination test must be supplemented by other serologic reactions, including the neutralization test, which is easily performed in tissue cultures.

Conclusions

The outbreak of influenza which occurred in the U. S. S. R. in the summer of 1957 was caused by strains of influenza virus differing in their antigenic pattern from previously known types. It was also possible to discern subgroups among the new strains which differ in avidity for their own group antibodies (the P, Q, and R variants of Mulder).

Human serums obtained in 1956 and 1957 prior to the epidemic had antihemagglutinins against the avid variants of the new strains, but not against the nonavid variants.

The neutralization test in tissue culture was found to be a more sensitive method for the determination of the level and shifts of antibodies against the new strains, since it detected antibodies against nonavid strains in serums which had no antihemagglutinins for these strains.

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HOSPITAL PRECAUTIONS AGAINST SPREAD OF ACUTE VIRAL HEPATITIS

Sidney Leibowitz, M.D., New York

Two forms of viral hepatitis exist, but identical precautions must be taken to prevent their spread to people caring for the sick. A set of precautions is here given for nurses, attendants, and technicians, especially as regards bedpans, bedclothes, dishes, thermometers, syringes, needles, and blood samples. An additional list of precautions applies especially to examining physicians, dental surgeons, operating surgeons, sigmoidoscopists, pathologists, roentgenologists, and especially anyone engaged in drawing blood, making injections, or handling materials liable to fecal contamination. Blood transfusions should be used sparingly; use of pooled plasma should be avoided if possible. Blood donors with a history or other evidence of hepatitis must be excluded. Gamma globulin should be available to persons who have been exposed to the danger of hepatitis. These precautions are especially necessary because the length of the incubation period (up to 180 days in cases of serum hepatitis) confuses the situation and casts doubt on the need for stringent preventive measures.

In recent years increasing awareness has existed among physicians, nurses, administrators, and allied medical personnel of the possible spread of acute viral hepatitis from hospitalized patients.[1] The reasons for greater interest in this problem are both medical and legal,[2] but primarily they stem from increased incidence of the disease. This is generally attributed to several factors: (1) heightened suspicion, resulting in readier recognition and diagnosis; (2) increased use of blood, blood products, and other parenterally given modes of therapy; and (3) existence of large numbers of unrecognized carriers.

At Beth Israel Hospital in New York City, the medical and nursing staffs have been continually alerted to understand and recognize the potentialities for spread of this infection, among themselves and patients, in the light of existing knowledge concerning its epidemiology. "Hepatitis precautions," to be applied when a patient with an identified or potential case of acute viral hepatitis is admitted to the hospital, have been in formal use for at least five years and for a longer period on a less formal basis. These rules and principles have been revised periodically. Most recently, they have been brought up to date in the following memorandum to the staff, reproduced here in its entirety with several minor editorial revisions made especially for this publication.

From the Medical Service, Beth Israel Hospital.

Background of the Problem

Two forms of viral hepatitis infection exist: infectious hepatitis (IH or virus A form, with a "short" incubation period of 15 to 40 days) and serum hepatitis (SH or virus B form, with a long incubation period of 50 to 180 days; this form is sometimes called "homologous serum jaundice"). The clinical pictures are indistinguishable. Neither results in immunity to the other. The IH form confers immunity to itself; the SH form often does not furnish this kind of immunity. Approximately half of the patients with viral hepatitis show no jaundice; admittedly, most hospitalized patients do because they represent those most sick.

Infectious hepatitis is communicable from person to person mainly by the fecal-oral route. It is believed that this virus enters the oral cavity and is excreted in the stools. Since this is the common means for transmission, the following prophylactic measures are essential: hygienic care in handling these patients; avoidance of close contact with them; care in handling their thermometers; care in disposal of feces; and sterilization of their bedpans after use. In addition, but less commonly, this virus is present in the blood stream and is transmitted from an infected person by use of insufficiently sterilized needles and syringes or by transfusion with whole blood or plasma of an infected person.

Serum hepatitis is transmitted solely by the parenteral route (from infected blood). The virus is not identified in the stools. Hence, in this type, prophylaxis is aimed at proper sterilization of needles and syringes, avoidance of use of contaminated instruments and needles, and, insofar as possible, transfusion with blood or plasma only where absolutely indicated.

Hepatitis is reportable to the local department of health, which is thereby in the best possible position to study the disease from epidemiologic and public health standpoints.

It is the responsibility of the physician in charge to indicate when his patient requires the precautions outlined here. Whenever there is a definite diagnosis of acute viral hepatitis or when the diagnosis of the patient's illness is still unresolved but a reasonable chance exists, in the evaluation of the responsible physician, that acute viral hepatitis may be the diagnosis, he shall be obliged to advise the nurse in charge to institute "hepatitis precautions." These precautions must be applied during the entire period of hospitalization.

Precautions in Handling Patients

Precautions for Nurses, Attendants, and Technicians.—Foremost are stool precautions, not unlike those taken in cases of typhoid fever, and some degree of patient isolation. The aim is not to handle the stool and to be careful with the bedpan. Soap and water cleansing of one's contaminated skin should be resorted to promptly. Contaminated linens should be segregated and specially laundered until sterile. Bed and mattress should be thoroughly cleaned after evacuation by a patient with hepatitis and aired at least overnight before use by another patient. The stool may be disposed of in the usual sanitary facilities. The bedpan should be assigned solely to the individual patient with hepatitis and thoroughly cleaned and carefully handled between uses until it can be sterilized (dry heat for two hours).

The patient should be isolated insofar as is practicable—short of employing gown and mask technique or bed net. During the first few weeks of illness (usually covering the period until recovery has begun), the patient is ordinarily confined to bed and utilizes a bedpan for moving his bowels. For the ambulatory patient, either a private toilet or a private (separate) commode should be available. The patient with hepatitis must not use toilet facilities in common with others.

Dishes and utensils should be handled with the isolation technique. Food remnants may be discarded in the ordinary way. Dishes and utensils which can be discarded after use should be used. Food attendants should handle these carefully while disposing of them. In this way, special dishes and utensils need not be assigned permanently to the patient with hepatitis for his or her exclusive use (as with thermometers) except, possibly, if a glass (and drinking tube) is provided for drinking or for storage of dentures. Such a glass should be sterilized as described below after discharge of the patient.

Each patient with hepatitis must have a thermometer for his sole use which shall be destroyed on his discharge. Rectal thermometers particularly are potent sources for transmitting the disease through careless handling. After contact with the thermometer, the attendant should immediately scrub his exposed hands copiously with soap and water with the usual aseptic technique (lever to draw water controlled by elbow or foot pedal).

Special care must be taken not to contact the blood of a patient with hepatitis directly or indirectly. A wound should be dressed with extreme care. Parenteral medication should receive extra attention. Needles for intravenous use should be removed with caution. Syringes and needles, when used, should be carefully washed and then deposited in a special receptacle prior to transmission to the central service department for necessary sterilization. After handling and washing such instruments, the individual should promptly wash his hands carefully with soap and water.

A separate needle and a separate syringe should be employed for each patient for any injection or drawing of blood. The multiple dose-per-syringe technique is prohibited for any inoculation or venipuncture.

Blood for blood cell counts should be obtained by means of the disposable lancet. The technician is urged to be careful not to contaminate himself with the blood of the patient.

Sterilization of needles, syringes, and instruments after use in a patient with hepatitis should, at a minimum, consist of boiling in water for not less than 30 minutes or autoclaving at 15 lb. of pressure for a minimum of 20 minutes. If dry heat is employed, the minimum is two hours.

Visitors should be limited, as feasible, by advising the patient of the communicability of the disease. Visitors should be warned against making intimate physical contact with the patient and sharing food and eating utensils.

Precautions for Doctors.—All the above nine precautions similarly apply, when appropriate, to the examining physician, dental surgeon, physician engaged technically with injection, drawing blood, or roentgenologic procedure, operating surgeon, sigmoidoscopist, and pathologist. When in doubt, the individual must apply soap and water promptly to the exposed skin.

In addition, the physician is urged to consider the following principles and measures: 1. Use blood transfusions sparingly and only where absolutely necessary. Pooled plasma should not be used if it can be avoided. When use of plasma is necessary, there is available a supply (in this hospital) which has been prepared by six months' standing at room temperature. 2. Blood donors should be selected with caution. Exclude those who give history or other evidence of hepatitis. 3. Prescribe gamma globulin to exposed persons as indicated. At present, persons with generally accepted indications are children, pregnant women, debilitated persons, and those exposed during an epidemic.

Gamma globulin, in addition, should be made available to any medical, nursing, or allied personnel who are unduly exposed. It should be borne in mind that gamma globulin has preventive effect only against the IH (virus A) form of viral hepatitis, although in most circumstances one cannot be certain of the type with which one deals. Therefore, all doubtful situations should be resolved by giving gamma globulin. The dosage of gamma globulin for prophylaxis should ordinarily be 0.01 to 0.02 ml. per pound of body weight, although up to 0.06 ml. per pound has been found more effective under certain circumstances.[3]

Conclusions

The hospital patient with acute viral hepatit presents a problem in potential spread of the di ease to staff members, to other hospital patient and even to visitors (the last factor is of sma magnitude in the over-all picture). Enough known about the epidemiology and mode of sprea of this infection to permit the drawing up of program aimed at preventing the occurrence secondary cases. This is possible despite the a knowledged failure to date to identify the causa tive agent directly.

Such precautions are particularly urgent becaus the prolonged incubation periods involved tend t nullify the need for special preventive measure against spread. The relationship between primar and secondary cases is not readily perceived b the average, untrained observer; in fact, most ofte the subsequent cases do not come to the attentio of the attendants of the initially infected person.

A program currently in use in a general hospita is presented here. It appears equally adaptable fo any institution which cares for patients. Althoug the precautions itemized here are centered aroun the hospitalized patient, similar principles appl to medical handling of persons in the home, th office, the clinic, the laboratory—in fact, whereve physicians, nurses, and technicians come in contac with patients, their body fluids, or their excretions

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Drs. Harry Vesell and Leon N. Sussman of the attendin staff and Miss Rose Muscatine and Mrs. Ethel Witkin o the nursing staff, Beth Israel Hospital, assisted in the formu lation of this program.

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SHORT OBLIQUE FRACTURE OF THE TIBIA

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In a series of 598 fractures of the tibia, 29 were found to be located near the junction of the middle and lower thirds of the bone. The level of the fracture in this group of cases was on the average 7.6 cm. proximal to the ankle joint. In spite of the homogeneity of this group, the methods of treatment were varied, the time at which union occurred could not be stated precisely, and the end-results ranged from early union with excellent function to repeated infection with ultimate amputation. Whether the fibula remained intact or was broken at the same time did not appear to affect the healing of the tibia, and tibial healing in the presence of a fibular fracture took just as long when the fibular fracture was high as when it was low. However, when tibial fracture line was short (e. g., 4.5 cm. in length as compared with 8 cm.) with a fibular fracture at the same level, the structure was extremely unstable. For such cases some type of internal fixation is recommended.

The short oblique tibial fracture in the adult, occurring at the junction of the middle and distal one-third, is most often associated with a fracture of the fibula. However, in spite of its rather common occurrence, little information regarding its incidence, mechanism, and treatment has accumulated in the literature. In previous reports, workers have by and large favored open reduction and internal fixation. In 1938, Linden[1] reported a large series of short oblique fractures of the tibial shaft (at all levels and in patients in all age groups, including the early teens) treated by immobilization with cast, traction, and immediate open reduction with screw fixation. He concluded that the latter therapy was the treatment of choice. Similarly, in 1941, Mansfield[2] reported 15 cases of the short, oblique, spiral fracture of both bones of the leg, treated by open and closed methods, and concluded that immediate open reduction with internal fixation was the treatment of choice. He observed the usual high location of the fibula fracture and concluded that this fracture was unimportant insofar as the treatment of the short oblique tibial fracture is concerned. All of the fractures in his series healed without complications. It is our belief that many of these factors are relatively stable and that perhaps in many instances, with proper selection of cases, nonoperative treatment may well be the treatment of choice.

Materials and Methods

During the past seven years (1949-1956) at the Veterans Hospital and the past four years (1952-1955) at the Jefferson Davis Hospital in Houston, Texas, 598 fractures of the tibia have been treated. Of this total number of cases, 29 (4.9%) of the patients had a short oblique fracture located at the junction of the middle and distal one-third. The end-results in all 29 cases were confirmed by x-ray examination, and we personally examined 25 of the patients. Additional information was obtained by talking with the surgeons who actually performed the operations and by examining the medical records and questionnaires. Finally, those patients in distant cities were examined and x-rayed by cooperating surgeons in nearby areas.

No fracture was included which occurred above a line, perpendicular to the shaft, 10 cm. above the ankle joint as measured on the x-ray (fig. 1). Similarly, no fracture closer than 4 to 5 cm. to the joint was included. The length of the tibial fracture line was felt to be important in delineating this fracture; and only the fracture lines 4.5 to 8 cm. in length were believed representative.

All procedures, open and closed, were carried out by the resident staff under supervision. When open reduction and fixation with plate was performed, the plate (see case 19 and fig. 4 and 5) was of the slotted type. In one case, however, a Lane plate was utilized. All plates were applied to the lateral aspect of the tibia, whenever feasible, with as little periosteal stripping as possible. Postoperatively, plaster immobilization was used in all cases of open reduction regardless of type of internal fixation.

The intramedullary rod (see case 13 and fig. 3) was of the triflange type, designed by J. Otto Lottes. In most cases, the rod was inserted just medial to the tibial tuberosity. In some cases the patellar tendon was split and the rod inserted directly in the middle of the tibial tuberosity in line with the tibial crest. The nailings and the reductions were under direct vision, with one exception.

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Screw fixation (see case 28 and fig. 6 and 7) was accomplished by the use of stainless steel screws of the Collison type. No attempt was made to place the screws at right angles to the cortex as advocated by Arzimanoglou.[3] A cast or splint was applied to every simple fracture immediately upon the patient's entrance to the hospital. Of those fractures treated by casting, three were wedged in an attempt to improve position. All cases were presented at the orthopedic staff conference, and those fractures whose position was unsatisfactory or whose stability was poor were openly reduced and internally fixed. Some fractures which might have been treated by closed methods later in the series were operated on in order to evaluate the triflange nail. All compound fractures were débrided initially and internally fixed.

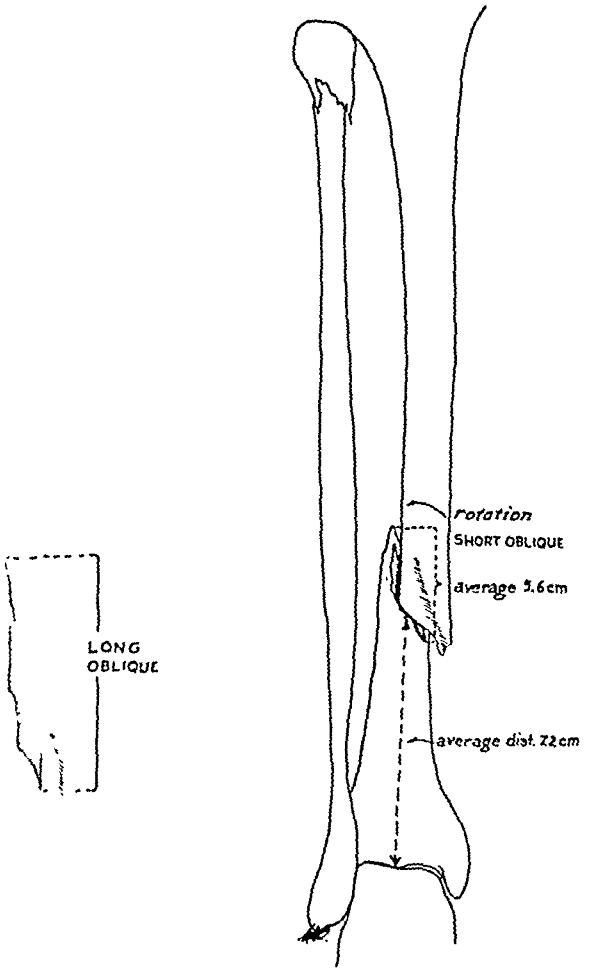

Fig. 1.—Diagrammatic representation of short and long oblique fractures of lower tibia.

Periosteal healing was judged to have occurred when a firm bridge of callus had appeared across the fracture site. Endosteal healing was considered to be present when there was continuity of the medullary canal and the fracture line was no longer evident. Infections were classified as superficial when the deep structures did not appear involved. When the infection was associated with systemic signs and with exposure of tendons and/or bone, it was classified as deep. Skin necrosis at the operative site was recorded as mild or severe. Severe necrotic lesions were those requiring skin grafts.

Results

Open reductions were performed in 21 of the total of 29 cases. All operations were performed at one of our hospitals. These 29 cases (100%) have been followed to their final outcome or up to the time of writing. The average follow-up was 35 months, the longest was 81 months, and the shortest was 12 months. No children were included in this study. The youngest patient was 27 years of age and the oldest was 80. The average age was 41.2 years. Twenty-two fractures occurred in males and seven in females. The right side was affected in 12 cases. No patient was encountered with bilateral short oblique tibial fractures. Approximately one-third of the fractures were produced by fighting and one-third by minor falls—such as falling down one or two steps. One case was produced by a horse falling on the leg; another, by falling through a door transom. Inebriation to a greater or lesser extent was present in 12 cases—or 40%. It is our feeling that these fractures are produced by torsion, the common example being that of throwing a punch and missing the target. The foot is apparently well fixed, so that when the body twists the proximal tibia, the short oblique fracture at the junction of middle and distal one-third is produced.

A thorough study of the configuration of the tibial fracture was made. The average length of the tibial fracture line was 5.9 cm., with the shortest being 4.5 cm. and the longest 8.0 cm. The closest distance to the ankle joint from the fracture line was 4.5 cm. and the longest was 10.0 cm., with the average being 7.6 cm. In a large percentage of cases (15 cases, or 50%), the distal fragment of the tibia was noted either originally or later to have a vertical fracture line. In two cases this fact was not appreciated and gave rise to moderate difficulty in securing adequate internal fixation. The fibula fracture level was studied, and in 62% of the cases the upper one-third was involved. In 16% the fracture levels were the same (L_3). In four cases the fibula was intact, while in two patients there were segmental high-low fractures. The fibula was comminuted in 72%, or 21 cases.

Examination of the x-rays taken on admission revealed only 0.25 in. shortening in 60% of the cases, and these were high fibula (U_3) fractures. The main deformity seemed to be rotation in this group. The four cases in which the fracture lines were at the same level were extremely unstable and tended to override markedly. There were three compound fractures. All were treated by initial débridement and some type of internal fixation. In two cases the triflange nail was utilized, and the remaining fracture was secured with two screws. Simple fractures were operated on as soon as the general condition of the patient permitted. The longest time from simple fracture to open reduction was 16 days. One patient was reoperated on after loss of fixation by initial procedure. From the table, it is possible to see that partial weight bearing was started slightly earlier in the cases treated by intramedullary rods. Full weight bearing was permitted earliest in the patient with plate and transfixing screw.

An accurate statement of the exact time at which periosteal and endosteal union occurred was impossible due to failure to obtain serial x-rays. Many patients did not return at the appointed times, and two patients did not even seek medical care after application of their initial cast. Endosteal healing had occurred in all cases except five at follow-up examinations. One patient had his leg amputated 14 months after the operation; one was wearing a brace without pain and had periosteal union when seen at 27 months, one was hospitalized with gross motion and possible osteomyelitis 23 months later; one was working without support as a bulldozer operator and had periosteal union; and one had periosteal union at 12 months, but the fracture line was still faintly visible

A study of the possible effect the level of the fibula fracture might have on tibia healing was made. It was felt that high fibula fractures (with more muscle support) would be more conducive to early tibial union than similar fractures with low one-third fibula fractures. However, no difference in healing time could be attributed to the fibula fracture level. No delay in healing was noted with the intact fibula. No primary bone grafts were performed. One patient with delayed union was reoperated on two years later in an effort to allow him to discard his leg brace and thus return to work. The fracture was united at operation Another patient was operated on because it was felt that there was nonunion. At operation, the fracture was united by a small bony bridge. Of the seven patients treated in casts, three were bedridden at the time of the injury. Two have not walked since, being confined to wheelchair and bed at all times. Two were chronic alcoholics who refused to cooperate, removing portions of their casts and braces at will.

Complications

Nonunion occurred in 1 of the 29 total cases. This patient failed to obtain primary healing of the operative wound, which drained for about four months. Fifteen months after injury, although there was no drainage from the operative site, callus was consistent in appearance with chronic osteomyelitis. Definite osteomyelitis occurred in one patient. An ill-advised wide ostectomy and plate removal was performed three months after injury. A fibula transplant procedure then failed, and 21 months after injury the leg was amputated.

Infection developed in one patient, with three-screw fixation, after leaving our hospital and being transferred to another hospital. Skin necrosis at the fracture site proved to be a very troublesome complication. Of a total of five patients, three with intramedullary rods had necrosis classed as mild, healing without skin graft. One of these patients had a compound fracture. The remaining patient, with an intramedullary rod, required a split graft at four months. One patient with a plate also had mild necrosis of skin over the operative site, which healed without difficulty.

Two patients developed transient nerve palsy postoperatively. One case involved the common peroneal nerve and was thought due to constricting cast. The other case involved hip, thigh, leg, and foot on the fracture side and was believed due to one-legged spinal anesthesia. Both recovered fully at four days and two months respectively.

Results of Operations in Twenty-nine Patients with Short Oblique Fractures of the Tibia

							Weight Bearing Started, Mo	
Operation	Cases, No	Amputations	Nonunion	Malunion	Osteomyelitis	Cellulitis	Partial	Full Unsupported
Casts	7	0	0	1	0	0	3.0	8.0
Rods . .	9	0	0	2	0	0	2.5	10.5
Screws . . .	5	0	0	2	0	1	3.6	9.8
Plate . . .	5	1	1	0	2	0	3.0	10.0
Transfixing screw and plate	1	0	0	0	0	0	3.0	6.0
Additional plate and screw	1	0	0	0	0	0	3.0	10.0
Traction	1	0	0	1	0	0	3.0	8.0
Total	29	1	1	6	2	1	Av 3.1	Av 9.9

Of the intramedullary rods, one was removed because of erosion of the tip through the skin at the tibial tuberosity. Two other rods had to be removed because of pain over the proximal tip of the rods. One plate (slotted type) broke and had to be removed at 15 months postoperative. One patient had to be reoperated on after loss of fixation occurred with use of a single screw.

Malunion was noted in a total of six cases treated by all methods. There were five varus deformities, varying from 10 to 20 degrees. One was treated with rod, two by screws, and one in traction. One patient with screw fixation was reoperated on and a plate was inserted, but it, too, failed to correct the alignment. One patient treated in a cast had 10 degree recurvation. There was not a single case of valgus or severe rotation deformity. None of the malunions were symptomatic at follow-up. Measurable shortening occurred in two cases. Plaster immobilization resulted in one instance in shortening of 0.5 in. and a Lottes rod in another of 0.25 in.

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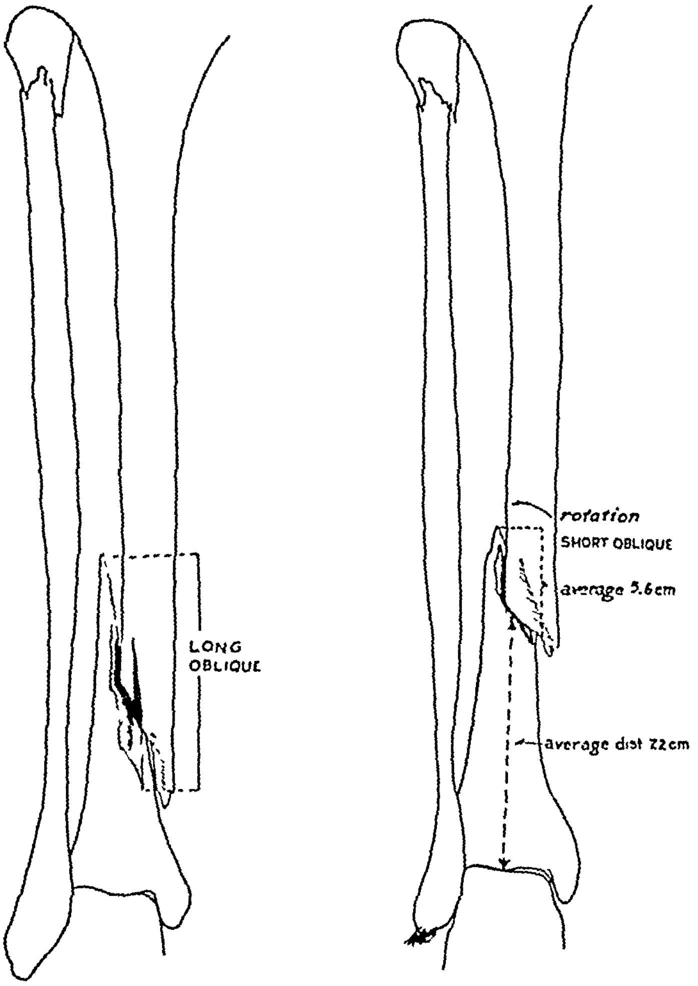

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CLINICAL NOTES

SUCCESSFUL TREATMENT OF MASSIVE AIR EMBOLISM PRODUCING CARDIAC ARREST

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Massive air embolism is a relatively rare catastrophe but often a lethal one. The occurrence of air embolism, massive enough to produce cardiac arrest, with a successful outcome seems to warrant reporting.

Report of a Case

A man aged 49 years was admitted to the hospital on April 27, 1957, shortly after receiving a gunshot wound from a .38-caliber pistol, the bullet having entered the left hip just superior to the left greater trochanter and having apparently coursed in a medial direction. On admission the patient was extremely apprehensive, intoxicated, and in severe hypotension, the blood pressure being 40/0 mm. Hg. The clinical examination revealed signs of peripheral vascular collapse, but physical examination otherwise was within normal limits. Palpation of the abdomen revealed it to be soft and nontender; bowel sounds were present. Therapy with intravenously given lactated Ringer's solution was begun, and x-rays of the left thigh and abdomen were then taken. No fracture was seen in the left femur; however, a chip fracture was present at the anterior lip of the left acetabulum. The bullet, which had entered laterally over the area of the greater trochanter on the left, was seen to be present over the left iliac fossa and far anterior on lateral film of the abdomen. It could not be ascertained whether the bullet was in the anterior abdominal wall or within the abdominal cavity.

On examination the urine was free of red blood cells; the urinalysis was negative. The pulse rate remained good at the femoral, popliteal, and posterior tibial arteries bilaterally. Rectal examination did not reveal the presence of any gross blood. However, during the period of observation, while the blood pressure was being elevated with the administration of a crystalloid solution, and during x-ray examinations, the patient was noticed to develop marked tenderness in the left lower quadrant with a suggestion of fulness in the left lower quadrant to deep palpation. The bowel sounds, which had been normally active, became absent over the ensuing hour of observation. At this time a diagnosis of intra-abdominal missile was made, and the bullet was thought to have passed into the abdominal cavity by virtue of being reflected off the acetabulum anteriorly and superiorly. At this time the blood pressure had been elevated to 100/70 mm. Hg and laparotomy was decided on. The abdomen was explored through a lower midline incision and about 300 cc. of fresh blood was encountered. The peritoneum was seen to have been perforated by the bullet, which had entered just lateral to the bladder and had then perforated the lower ileum at one point. The bullet was found lying free in the abdominal cavity. Further exploration of the extraperitoneal area revealed that there was a through-and-through injury of the external iliac vein, which destroyed the bulk of the vein wall; bleeding from this area was brisk.

No other injury to surrounding structures, including ureter and external iliac artery, was found. Repair of the vein was thought impossible, and consequently the external iliac vein was doubly ligated with suture ligatures and the perforation of the ileum was closed with interrupted cotton sutures. Exploration of the remainder of the abdominal cavity was entirely within normal limits; consequently, the abdomen was closed in layers. During the procedure the patient received an additional 1,500 cc. of lactated Ringer's solution and 1,000 cc. of whole blood. An estimated blood loss at the time of surgery was about 1,200 cc. At the completion of the operation the left leg was elevated, sheet wadding was applied, and the leg was wrapped in elastic bandages. The patient was then sent to the recovery room in good condition, his blood pressure at that time being 120/85 mm. Hg. As the patient was moved from the operating table to the recovery room bed he suddenly had a sharp fall in blood pressure and became cold and clammy, and blood was seen to be oozing from the drain sites, which had been left lateral to the peritoneum, above the vein injury. Whole blood transfusion was again immediately started, this time intravenously at a rapid rate with use of the air bulb for pressure, and the patient was returned to the operating room. The previously made wound was then opened, and blood was seen to be coming from the femoral canal around the area of the previous ligation of the external iliac vein. On closer inspection, however, the bleeding was not coming from the previously severed and ligated end of the vein but apparently from the common femoral vein, which had been injured at a level lower than the area of ligation. This bleeding was then controlled by digital pressure; the patient was at this time receiving blood under pressure in two cut-down sites in the legs.

Now a loud gurgling sound was heard; on inspection it was seen that the blood that had been under air pressure in the transfusion bottle was all absorbed and the patient had received a massive dose of air intravenously. This bottle was promptly disconnected, and in about 10 seconds the anesthesiologist noticed that the patient had no blood pressure or pulse and was not breathing. Palpation of the abdominal aorta directly at this time revealed no pulse. The head of the table was then lowered to deep Trendelenburg position, and within 15 seconds the left side of the chest was opened through an intercostal incision between the fourth and fifth ribs. The heart was tremendously dilated and in complete arrest, and during manual compression it felt like a large

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From the Department of Surgery, University of Texas, Southwestern Medical School.

bag of air, having no contractile ability. Because of this, a large no. 13 needle was inserted into the anterior surface of the right ventricle and an attempt was made to withdraw air with a 20-cc. syringe. The air came out under such pressure that the plunger was literally blown out of the end of the syringe, and the air whistled through the needle and syringe in its exit from the right ventricular cavity. After this, the needle was removed and the heart was massaged. Again, it did not assume a normal rhythm spontaneously, so 10 cc. of 1% procaine solution containing 1 cc. of 1:1,000 epinephrine solution was introduced directly into the cavity of the left ventricle. Manual systole was continued and in about 10 seconds a normal sinus rhythm of 60 beats per minute was obtained. Within an additional 15 seconds the blood pressure was obtainable at 40/0 mm. Hg, and in the ensuing two minutes this rose to 90/40 mm. Hg. At this time the no. 13 aspiration needle hole in the right ventricle was spurting blood with each systole, and consequently this was closed with a single suture of 00000 Deknatel arterial silk.

The patient was then breathing spontaneously, maintaining blood pressure and cardiac rhythm. Consequently the chest was closed, chest tubes were inserted, and the previous bleeding site was then reattacked. An incision was then made over the femoral canal in the leg, and the site of the lower perforation of the common femoral vein was then identified and closed with 00000 arterial silk suture without incident. The abdominal and leg wounds were then closed, and the patient returned to the recovery room in good condition, maintaining a blood pressure at that time of approximately 90/60 mm. Hg. The patient had, by this time, received a total of 12 pints of blood and 4 liters of lactated Ringer's solution. He was awake by the end of the second procedure, and his blood pressure promptly rose to 110/80 mm. Hg, where it was well maintained. The postoperative course was complicated only in that on the second day postoperatively he developed paroxysmal auricular tachycardia, which was well controlled easily with digitalis. Chest tubes were removed on the fourth postoperative day and, after an episode of delirium tremens controlled by alcohol given intravenously, the patient began eating, was ambulatory, and otherwise had an uneventful postoperative course.

Comment

Massive air embolism occurred during the infusion of whole blood under positive pressure while the patient was momentarily left unattended. The ensuing air embolism was so massive that it caused cardiac arrest and respiratory arrest within 15 seconds. The amount of air that was given was estimated to be in excess of 300 cc. in a period of a very few seconds. At the time this catastrophe occurred the patient was immediately put into Trendelenburg position and we contemplated turning him on his left side as recommended by Durant, Long, and Oppenheimer [1] in their experimental work published in 1947. However, this air embolism was so rapid and so massive that cardiac and respiratory arrest occurred before this maneuver could be attempted. Consequently, the chest was opened and cardiac massage begun within 30 seconds after the occurrence of the cardiac arrest. This, however, was not effective as long as the right ventricle was over distended with the tremendous quantity of air. Needle aspiration of the right ventricle relieved the air block, and massage of the heart then produced an effective volume output. In less than a minute a regular cardiac rhythm had been restored, and blood pressure returned promptly. This method of therapy, although unknown to us at the time this catastrophe occurred, had been well outlined by Nicholson [2] in an excellent review of the etiology, diagnosis, and therapy of air embolism.

To substantiate and repeat the method of therapy as has been outlined by Nicholson, the essential steps should include (1) withdrawal of the needle and discontinuance of the source of the air embolism; (2) lowering of the head to prevent air from entering the cerebral circulation in the event that arterial embolism may have occurred; (3) the placing of the patient in a left lateral position as recommended by Durant so that the air block may be released, if there is time for this maneuver; (4) if cardiac arrest occurs or the air embolism is too massive for this maneuver to succeed, the performance of emergency thoracotomy with needle aspiration of the right ventricle followed by cardiac massage as was employed in this case is not only necessary but essential for preservation of life; and (5) maintenance of a clear airway and establishment of continued effective artificial respiration with oxygen. This was carried out in the reported patient.

Air was looked for in the left side of the heart with the thought that possibly the patient had an undiagnosed patent foramen ovale or congenital interventricular septal defect. No air, however, was seen in the coronary arteries at any time, and in view of the fact that the patient responded promptly it was felt that he had received air only in the right side of the heart. It should also be pointed out that this catastrophe can be prevented in the future, as plastic blood containers that contain no air are now becoming available.

Summary

A patient with massive air embolism that produced cardiac and respiratory arrest was successfully treated. Essential in the successful treatment of air embolism of such a magnitude is immediate emergency thoractomy with needle aspiration of air from the right ventricle and manual cardiac massage to correct the cardiac arrest. It is hoped that this additional article will call the attention of surgeons to the available methods of therapy of massive air embolism when this fortunately infrequent but often fatal catastrophe occurs.

5323 Harry Hines Blvd. (19).

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MULTIPLE MYELOMA IN SIBLINGS

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and
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We have had occasion to observe the occurrence of multiple myeloma in two siblings. These patients were not twins. We are unaware of any previous report of this disease occurring in siblings. None of the approximately 550 patients suffering with multiple myeloma seen in the past at the Mayo Clinic [1] were siblings.

The criteria for the diagnosis of multiple myeloma are well established and need not be repeated here. The value of urethan (ethyl carbamate) in the treatment of some cases of multiple myeloma has been reported by a number of investigators. Kenny and Moloney [2] reported the long-term use of urethan in three cases of multiple myeloma. Two of their patients were alive and well 11 years after administration of the drug was begun, and the third patient was alive 9 years after he first received urethan. These investigators emphasized that in all three cases the myeloma cells were of the mature type and that this, rather than the administration of urethan, might have accounted for the benign, chronic course of the disease.

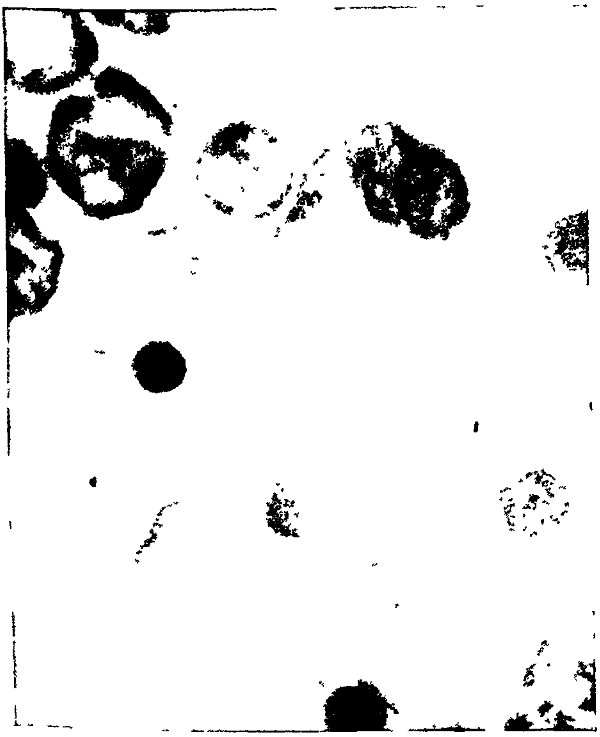

Fig. 1 (case 1).—Photomicrograph of bone marrow (× 800). Note myeloma cells.

In the two cases reported here, the myeloma cells also were of the mature type. One patient (case 1) was advised to take urethan, but refused to do so because it caused nausea and vomiting. This patient died. His brother (case 2) has taken 1 Gm. of urethan three times daily for more than a year and is in excellent general condition at the time of writing. Reports of these two cases follow.

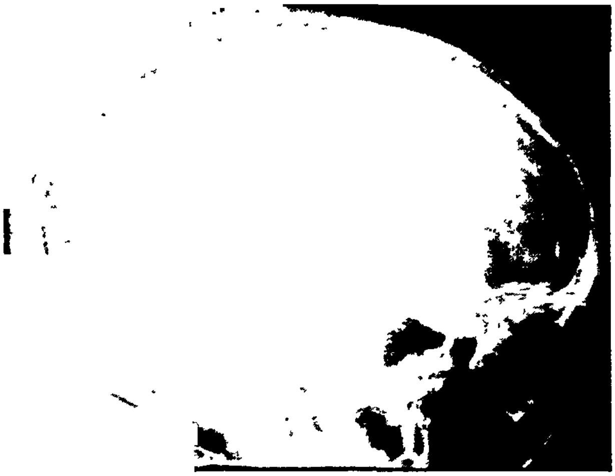

Fig. 2 (case 1).—Roentgenogram of skull, showing areas of rarefaction in right frontal area.

Report of Cases

Case 1.—The patient was a 53-year-old male, first seen by one of us (W. E. H.) at the Mayo Clinic on Oct. 6, 1952. In mid-March of that year he had developed severe pain in the lower part of the back, radiating to the right and left lumbar areas, which was aggravated by movement, coughing and sneezing, and lifting and bending. The pain was so severe that the patient had discontinued his work as a banker about April 1. Roentgenographic examination of the spine at his local hospital had been reported to reveal "cystic change in the fifth lumbar vertebra." He had worn a back brace since mid-April. Three weeks prior to his admission, microscopic hematuria had been noted. He had been told that he had a "chronic blood condition" and had been given 2 Gm. of urethan daily. However, he had stopped taking the drug, since it caused nausea and vomiting. For three weeks before admission he had had soreness in the right hip. He also had noticed shooting pains in the right foot, particularly in the three middle toes.

The general physical examination was negative, except for limitation of motion of the lumbar spine and muscle spasm. The patient's weight was 177 lb. (80.3 kg.). His blood pressure was 120 mm. Hg systolic and 74 mm. Hg diastolic. Urinalysis revealed grade 4 (on a basis of 1 to 4) albuminuria and grade 4 erythrocyturia on two occasions. The test for Bence-Jones protein in the urine was not conclusive, due to the presence of blood. The concentration of hemoglobin was 12.4 Gm. per 100 cc. of blood. The erythrocyte count was 3,680,000 and the leukocyte count 4,800 per cubic

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From the divisions of medicine, Lexington Clinic (Drs. Herrell and Ruff), and Mayo Clinic (Dr. Bayrd).

millimeter of blood, with 21.5% lymphocytes, 9.5% monocytes, and 69% neutrophils. There was 26 mg. of urea per 100 cc. of blood. The Kline test for syphilis was negative. The sedimentation rate was 67 mm. in one hour (Westergren method). Blood smears showed grade 2 rouleaux formation and occasional myeloma cells. The total serum protein level was 7.91 Gm. per 100 cc. The albumin level was 3.31 Gm. per 100 cc. and the globulin 4.60 Gm. per 100 cc. Examination of the sternal marrow disclosed findings typical of myeloma (fig. 1). Roentgenographic examination of the chest was negative. A roentgenogram of the lumbar spine showed a destructive lesion involving the fifth lumbar vertebra with partial collapse. A second lesion was noted in the right ilium, which was partially obscured by gas but was thought by the roentgenologist to be due to myeloma. A roentgenogram of the skull showed an area of rarefaction in the right frontal bone and other vaguely outlined areas of rarefaction (fig. 2). An attempt to do a left retrograde pyelogram was unsuccessful, because an obstruction was met in the left ureter.

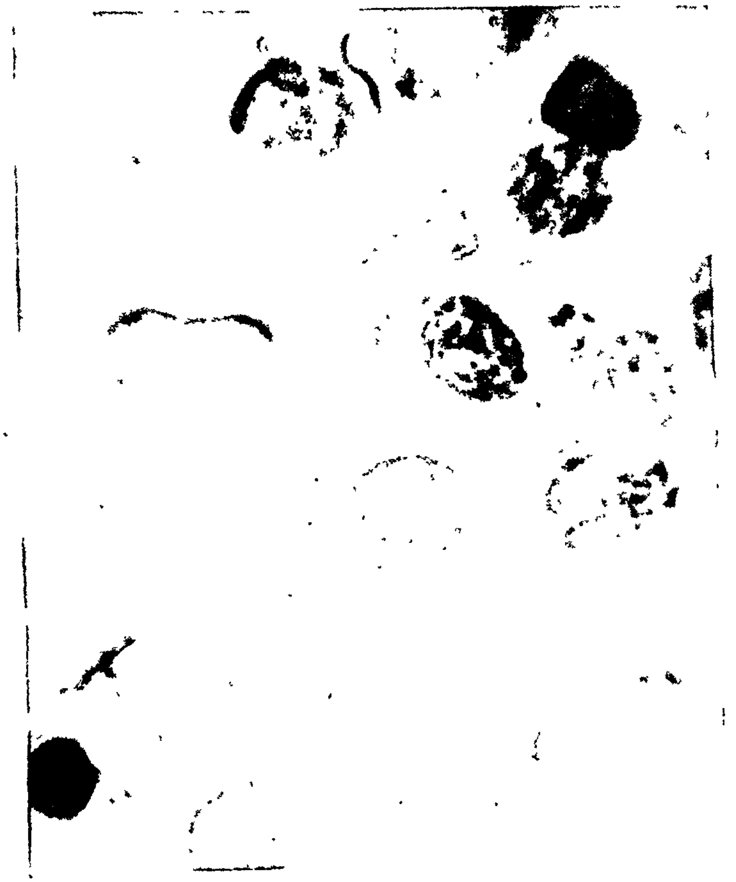

Fig. 3 (case 2).—Photomicrograph of bone marrow (× 800), showing one myeloma cell with double nucleus.

The patient was advised to continue taking full doses of urethan, which, as already has been stated, he failed to do. Within a few months he was bedridden, and he died at his home six months after dismissal.

Case 2.—The patient was a 55-year-old male, first seen at the Lexington Clinic on Oct. 8, 1956. His family history, as in his brother's case, was negative, except that their mother had died years ago of pernicious anemia. The patient had had a foreign-body, giant-cell tumor removed from his left tibia at the Mayo Clinic in 1939. There had been no recurrence. The patient's complaint was "back pain," which had occurred intermittently since 1950. He had had an attack of acute back pain in 1950 and had worn a cast for three months, after which his pain had subsided. In 1952, he had had severe pain in the lumbar region, lasting approximately four weeks. In June, 1956, while working in his yard the patient pushed down hard on a shovel, which broke, causing him to fall. He immediately experienced severe pain in the lumbar area with "muscle spasms." He was unable to work for approximately three weeks. He then resumed his occupation as a traveling salesman, but in mid-July, 1956, the pain became so severe that he again stopped working. The pain was located in the lumbosacral area and spread across both hips and upper lumbar areas, similar to that described by the patient's brother. Coughing and sneezing produced a knife-like pain in his back. The only diagnosis that had been made was "back strain."

The general physical examination was negative, except for marked limitation of motion of the lumbar spine with muscle spasm and absence of the ankle-jerk reflexes bilaterally. The patient's weight was 162 lb. (73.5 kg.); his normal weight was 170 lb. (77.1 kg.). His blood pressure was 120 mm. Hg systolic and 80 mm. Hg diastolic. Urinalysis revealed 3+ albuminuria. The test for Bence-Jones protein in the urine was positive. The hemoglobin concentration was 11.9 Gm. per 100 cc. of blood. The erythrocytes numbered 3,860,000 per cubic millimeter of blood and the leukocytes 6,200. The differential count revealed 51% neutrophils, 34% lymphocytes, 6% monocytes, and 10% eosinophils. The Kahn test for syphilis was negative. The sedimentation rate was 112 mm. in one hour (Westergren method). The total serum protein level was 7.68 Gm. per 100 cc. The albumin level was 3.1 Gm. and the globulin 4.58 Gm. per 100 cc. Examination of smears of peripheral blood revealed marked rouleaux formation with eosinophilia. The sternal marrow appeared typical of myeloma, with rather mature cells (fig. 3) Electrophoretic studies of the serum and urine disclosed changes characteristic of myeloma. A roentgenogram of th chest was negative. Roentgenographic examination of th lumbar spine and pelvis revealed marked demineralizatio with wedge deformity of the third and fourth lumbar vertebrae. A roentgenogram of the skull revealed demineralization and areas suggestive of myeloma (fig. 4).

The diagnosis of multiple myeloma seemed adequatel established. The patient was advised to take 1 Gm. o urethan three times daily and was dismissed on Oct. 1 1956. He took the drug unfailingly and after returning hom began to improve. He also was fitted with a chair-bac brace, which he has continued to wear.

Fig. 4 (case 2).—Roentgenogram of skull, showing multiple areas of rarefaction.

The patient returned to the Lexington Clinic on Oct. 7, 1957. He was working full time. He stated that he had had no further back pain and felt better than he had in five years and that he had a good appetite and took the urethan with his meals. He had gained 8 lb. (3.6 kg.) in weight The general physical examination was negative, except for some limitation of motion of the back. The hemoglobin measured 12.7 Gm. per 100 cc. of blood, and the erythrocyte count was 4,120,000 per cubic millimeter. Urinalysis showed only a trace of albumin. The test for Bence-Jones protein in the urine was negative. The total serum protein value was 8 6 Gm. per 100 cc. The sedimentation rate was 95 mm. in one hour. A roentgenogram of the chest was negative. Roentgenographic examination of the lumbar spine showed no change when compared with that made one year previously. The patient was in excellent general health and was happy with the result of treatment, particularly in view of his firsthand knowledge of the course of his brother's illness.

Comment.—The response to urethan therapy in this case is gratifying and consistent with the scattered reports on the effectiveness of this drug in the treatment of multiple myeloma that have appeared in the literature.

Summary

Two cases of multiple myeloma occurred in siblings. In both cases the myeloma cells were of the mature type. One patient did not survive, but was unable to tolerate urethan therapy. The other patient is alive and clinically well after being on urethan therapy for a little more than a year. We are unaware of any previous report in the literature of multiple myeloma occurring in siblings.

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PSEUDOTUMORS OF GASTRIC ANTRUM IN PERNICIOUS ANEMIA

REPORT OF A CASE

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and
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Changes in the radiologic appearance or pathological findings of the gastric antrum and pylorus in untreated pernicious anemia are rarely observed, but well-documented, phenomena. Most of the reports in the literature concern cases of pyloric hypertrophy discovered during routine postmortem studies on patients who died of pernicious anemia before treatment with liver or liver extracts became available.[1] However, in 1935, Baštecký and Váradi[2] reported two patients with proved pernicious anemia with pseudotumors of the antral region, found on radiologic examination, which disappeared on treatment with liver extract. Our purpose is to report a similar case of radiologic antral deformity in a patient with proved pernicious anemia, where the evidence was so convincing that surgery was performed under the impression that the patient had antral carcinoma.

A 67-year-old male was admitted to the hospital on June 5, 1957, complaining of weakness. Prior to admission, his physician had given him 2 pt. (1,000 cc.) of blood intravenously and had ordered an upper gastrointestinal series, which was reported as showing carcinoma of the stomach. On admission he denied having gastrointestinal symptoms but still complained of weakness. Initial physical examination revealed little of note except for moderate atrophy of the surface of the tongue. His blood pressure was 105/70 mm. Hg, his pulse rate 76 and regular, and his respiration rate 20. The neurological examination was within normal limits.

The initial blood studies showed a hemoglobin level of 6.2 Gm. per 100 cc., a red blood cell count of 2,010,000 per cubic millimeter, and a white blood cell count of 4,200 per cubic millimeter, with 37% polymorphonuclear leukocytes, 50% normal lymphocytes, and 13% eosinophils. One stool was negative for occult blood. A platelet count was 86,000 per cubic millimeter, and prothrombin time was 100% after the patient was given 1,000 cc. of blood. On June 12, 4 pt. (2,000 cc.) more of blood was given, with a rise in the hemoglobin level to 13.7 Gm. per 100 cc., a hematocrit of 43%, and a platelet count of 30,000 per cubic millimeter. A bone marrow aspiration on June 13 showed many megaloblasts and was interpreted as showing "megaloblastic anemia, probably pernicious anemia." A Schilling test with radio-active vitamin B_{12}[2A] on June 17, 1957, showed urinary excretion of only 2.5% of the labeled vitamin B_{12} dose. No free acid was found on fractional gastric analysis with histamine.

At the time of admission, an x-ray of the chest was negative, and an upper gastrointestinal series was read as showing "carcinoma of the gastric antrum with shallow ulceration and extension along the stomach wall to well above the incisura angularis" (fig. 1). No obstruction was noted. The patient was completely asymptomatic after transfusions; he ate well and seemed in good health. A second upper gastrointestinal x-ray series on June 25, 1957, three weeks after the first, was read as showing "irregularity and rigidity of the walls of the distal antrum, extending proximally along the greater curvature anteriorly to the angularis, but only a few centimeters proximally along the lesser curvature. The mucosal pattern is obliterated in this area. The pyloric channel is elongated. Conclusion: Carcinoma of the antrum of the stomach" (fig. 2). A gastric washing was negative for abnormal cells. On gastroscopy, there were marked generalized atrophic changes of the gastric mucosa, but no tumor was visualized in the antrum, and no ulceration was seen.

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The patient was started on therapy with vitamin B_{12} on June 19, with 100 mcg. given intramuscularly on alternate days, and placed on a diet of soft, bland foods. He continued to do well and was up and about without difficulty. Because of the definite x-ray findings, which had failed to change appreciably over a three-week period, exploratory laparotomy was carried out on July 5, at which time no tumor was found. The antrum was studded with mucus-containing cysts, and one of these was excised for pathological examination, the stomach then being closed without resection. The excised specimen was reported as showing a mucous cyst lined by columnar epithelium, with atrophic overlying mucosa. A neighboring lymph node, also resected, was negative for tumor. Convalescence was uneventful, and he was discharged on July 13, 1957. On follow-up examination on Sept. 24, 1957, he was completely asymptomatic and appeared in good health and spirits. Vitamin B_{12} therapy had been continued by his referring physician. Hematological examination showed a hemoglobin level of 15 Gm. per 100 cc. and a white blood cell count of 6,000 per cubic millimeter, with a normal differential count and normal-appearing red blood cells. A repeat upper gastrointestinal x-ray series was read as showing irregularity of the antral outline, with exaggeration of the mucosal folds. The antral systole was complete, although irregular, and there was no rigidity of the gastric wall. The findings were felt to represent chronic hypertrophic antral gastritis (fig. 3).

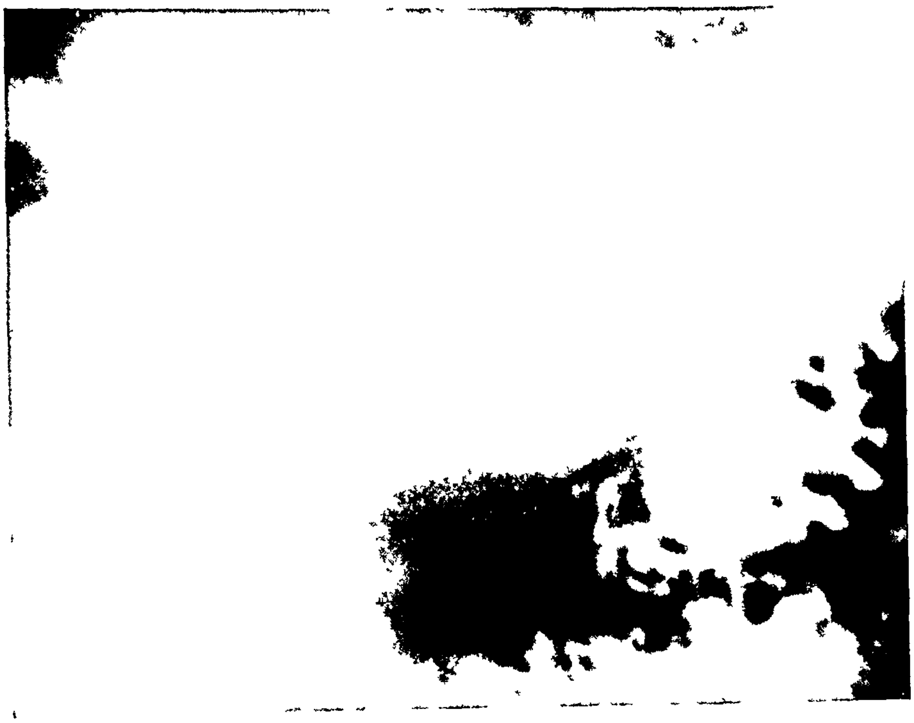

Fig. 1.—Roentgenogram showing initially discovered gastric antral deformity.

Comment

A search of the recent literature has failed to reveal reports of pseudotumors or hypertrophy of the pylorus associated with untreated pernicious anemia. Koch,[1b] in 1915, described 12 cases of pyloric hypertrophy, 3 of which occurred in untreated patients with pernicious anemia and were verified by postmortem examination. Kleemann,[1a] in 1919, gave a detailed history of a case in which the pyloric deformity was diagnosed by x-ray examination prior to death and confirmed on postmortem examination as actual pyloric hypertrophy. Mayeda,[1c] in 1921, described a fifth instance in which the patient died untreated and pathological study showed hypertrophy of the pylorus. In 1935, Bašteckÿ and Váradi [2] observed two patients with proved pernicious anemia who on x-ray examination of the stomach showed deformities almost diagnostic of carcinoma of the antrum and pylorus. They astutely noted, however, that the deformity of the antrum was not entirely constant on repeated examination and that there was an unusual irregular contour to the stomach borders. Both patients were treated nonsurgically with liver extract (it then being available), with reversal of the hematological picture and change of the x-ray appearance to normal. In one patient, this change occurred in less than a month. These authors felt that in their patients there was no actual pyloric hypertrophy, postulating instead, a spasm of the mucosal musculature without participation of the stomach musculature. They admitted that this was only a hypothesis, which they would find it difficult to support with facts. They also stated that they felt the x-ray picture was characteristic enough, when found in patients with pernicious anemia, to permit observation of the deformity during therapy of the anemia, with the expectation that the changes would revert to normal with remission.

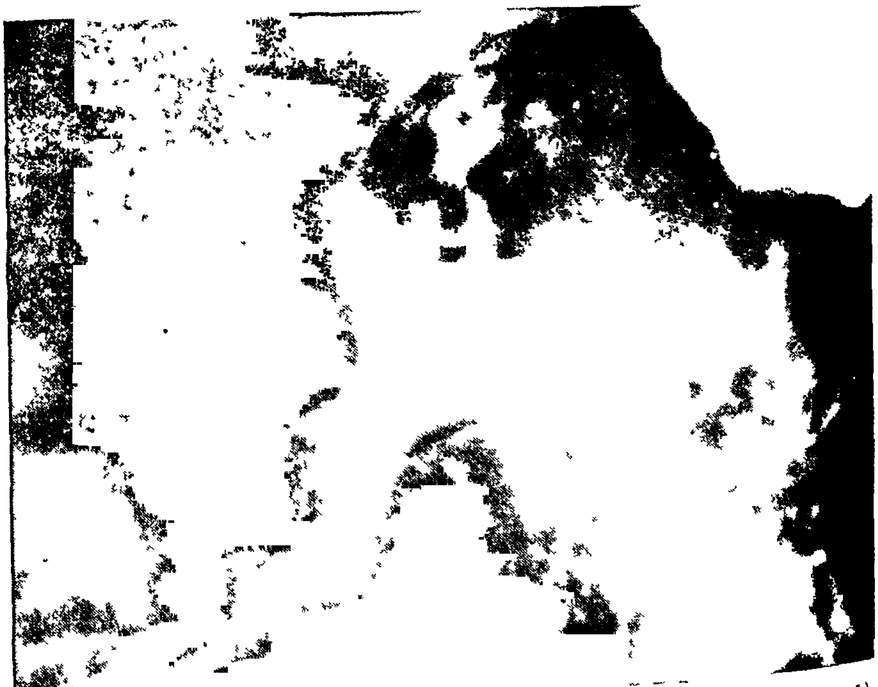

Fig. 2.—Gastric antral deformity seen 22 days after first x-ray series (fig 1)

In our patient, even though there was excellent hematological remission by the time of the second x-ray examination, there was so little change in the stomach outline that the roentgenologist had no hesitation in diagnosing carcinoma of the antrum. Almost three months later there was still some deformity, but this was read as gastritis and may easily have been caused by the numerous cysts of the antrum found at operation. These cysts were felt to be a logical result of the gastric mucosal atrophy, with repair and healing of the mucosa.[3]

Fig. 3.—Appearance of gastric antrum after three months of parenteral vitamin B_{12} therapy.

The marked deformity previously noted was not present. In commenting on the scarcity of reports concerning this condition, we note that none were found after 1935, when treatment of pernicious anemia with liver and liver extracts was well established, and that cases of true hyperthrophy were seen only in untreated patients dying of their disease. If muscular spasm does in time cause hypertrophy of the pylorus in untreated patients, and if this is reversible by therapy in the early stages, it is possible that widespread use of "antianemic" preparations, which frequently mask the picture of pernicious anemia today, have made such observations as ours an extreme rarity. In two other untreated patients recently observed, however, upper gastrointestinal x-ray series were entirely normal. Pseudotumors of the antrum would appear to be quite rare in pernicious anemia even without therapy.

Summary

A case of pseudotumor of the gastric antrum was discovered by x-ray in a patient with untreated pernicious anemia. The deformity persisted during two radiologic examinations. Exploration was done, and no tumor was found. After treatment with vitamin B_{12}, much of the radiologic deformity disappeared. Several such cases were reported in the literature prior to 1935.

6723 Bertner (25) (Dr. Nelson).

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CHANGING ASPECTS OF VENEREAL DISEASE.—The reduction in venereal diseases since the second world war probably owes more to favourable social conditions than to new remedies. In respect of only one disease, syphilis, is there evidence of considerable success in the campaign for control; and even for syphilis the ultimate outcome remains in doubt. Gonorrhoea threatens again to become very serious, and solution of the major problem of non-specific genital infection is not in sight. There are reasons for thinking that the incidence of lymphogranuloma venereum and even of granuloma inguinale may be increasing. The post-war decline in incidence, and the introduction of new remedies, have inspired a false confidence and a move to dismantle some of the organization which has served the public well in the control of these diseases. Because of this attitude it has been difficult to recruit young men of quality to this special subject. There is a case for strengthening rather than weakening the venereal-diseases scheme and for offering encouragement to new entrants by filling vacant appointments with venereologists and by financing research.—Ambrose King, "These Dying Diseases": Venereology in Decline? *Lancet,* March 29, 1958.

BACTERIAL ENDOCARDITIS DUE TO PSEUDOMONAS AERUGINOSA

REPORT OF A CASE

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and
Anna K. Knapp, M.D., Chicago

Bacteremia due to Pseudomonas aeruginosa was a rarity until the era of modern antibiotics. In recent years many cases of bacteremia due to this micro-organism have been reported, doubtless due to the unusual resistance of this bacterium to all of the antimicrobial agents in common use. The present case is unique in that there was marked vegetative endocarditis of the aortic valve. Our search of the literature indicates that it is the 10th case of endocarditis due to Pseudomonas aeruginosa to be reported.

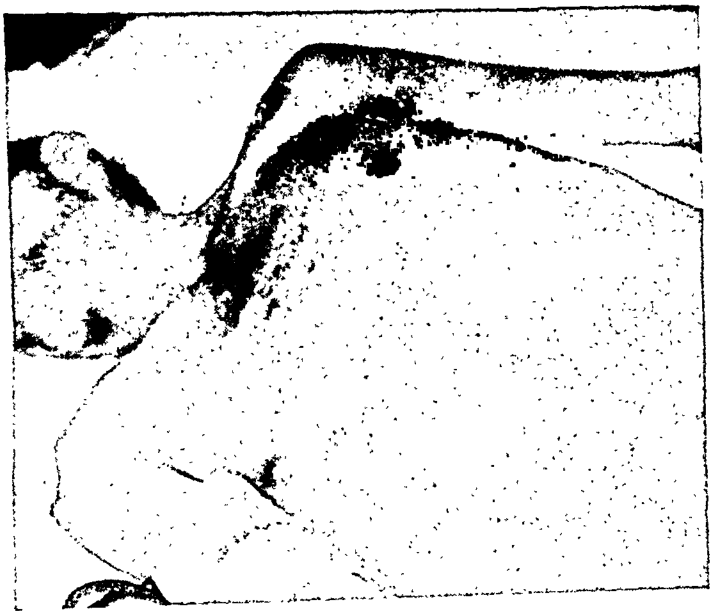

Fig. 1.—Photograph taken on 16th hospital day, showing petechiae over trunk and upper extremities.

The patient was a 23-year-old male narcotics addict admitted to the service of one of us (P. S. R.) in July, 1956. Since childhood he had had attacks of rheumatic fever, the exact number being uncertain. He admitted having given himself an intravenous injection of heroin two weeks prior to the time he was seen by us. When first seen by us he was complaining of pain in both small and large joints. Fever had been present for at least several days. Over the preceding week there had been one episode of vomiting; there was some abdominal distress. No bowel movement had occurred without an enema over the preceding week. His voice had gradually become weaker until he could speak only in a whisper.

The patient's temperature on admission was 99.8 F (37.7 C), his respiration rate 22 per minute, his pulse rate 94 per minute, and his blood pressure 130/68 mm. Hg. Physical examination revealed a well-developed, slender male in acute distress. He was dyspneic, somewhat orthopneic, and rather apathetic. The lungs were clear. The apex beat of the heart was in the midclavicular line in the fifth interspace and was regular. Diastolic and systolic grade 4 murmurs were heard best in the mitral area but were clearly audible over the entire precordium. Twelve hours after admission these murmurs had changed to only a diastolic grade 4 murmur heard best in the second and third interspaces on the left. There was no peripheral edema. Muscle guarding was noted in the right upper quadrant and interfered with accurate estimation of the size of the liver. Passive motion of the lower extremities caused pain.

Admission urinalysis gave normal findings. The hematocrit was 44%, and there was leukocytosis (20,000 leukocytes per cubic millimeter), with a differential count of 71% segmented neutrophils (many with toxic granules), 20% unsegmented neutrophils, and 9% lymphocytes. A corrected erythrocyte sedimentation rate was 5 mm. per hour. Roentgenograms of the chest showed some cardiomegaly, but there were no infiltrates in the lungs or significant engorgement of pulmonary vessels. Roentgenograms of the abdomen showed much enlargement of the liver and moderate splenomegaly.

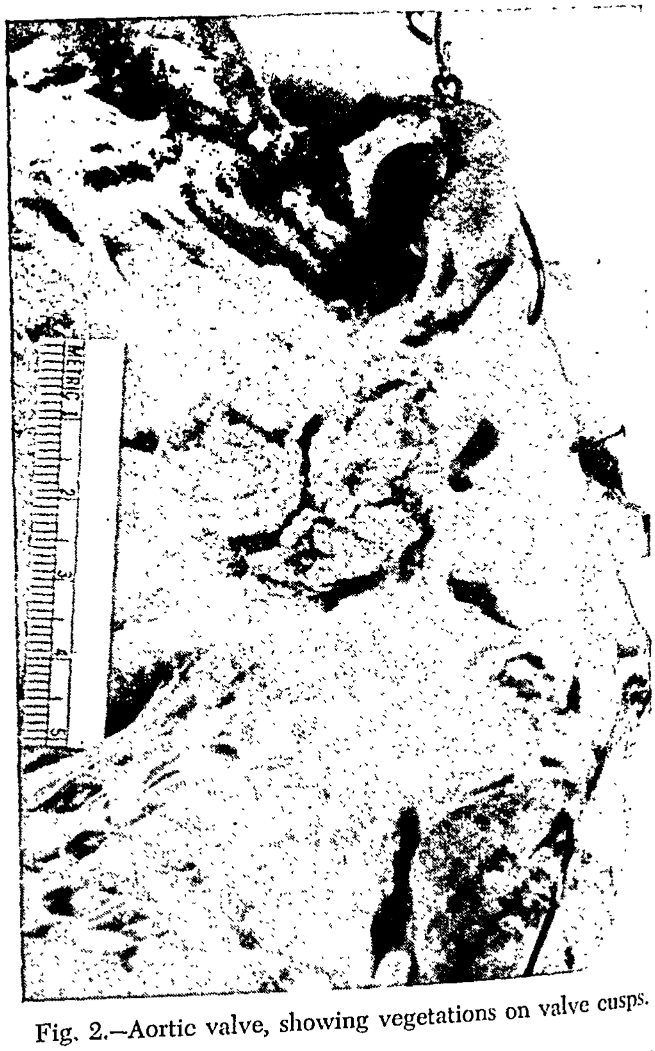

Fig. 2.—Aortic valve, showing vegetations on valve cusps.

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There were many amorphous collections of calcium within the liver. An electrocardiogram taken on the second hospital day revealed nonspecific changes. Agglutination tests done on the third hospital day for typhoid, paratyphoid, Brucella, and Proteus X-19 (Weil-Felix test) were all negative.

On admission a culture of a blood specimen was made, which on the third hospital day was positive for Pseudomonas aeruginosa. It was found to be most sensitive to dihydrostreptomycin and polymyxin B. Therapy with penicillin had been started in a dosage of 2,400,000 units per day on admission. When the sensitivity studies were reported on the third hospital day, the antibiotics were changed to polymyxin B (Aerosporin), 200 mg. intramuscularly daily (in four equally divided doses), dihydrostreptomycin, 1.0 Gm. intramuscularly daily (in two equally divided doses), and chlortetracycline, 0.5 Gm. intramuscularly twice daily. Since there was no clinical improvement after three days, sulfisoxazole, up to 8 Gm. daily, was given also. It was without effect, and its use was discontinued after six days. There was a spiking fever with temperatures ranging between 100 and 106 F (37.8 and 41.1 C) throughout the hospital course. Four blood cultures made during the polymyxin B therapy were negative. On the 10th hospital day, however, the therapy with polymyxin B was discontinued because of albuminuria. A blood culture made on the 11th hospital day was positive for Ps. aeruginosa. A lumbar puncture was done on the third hospital day. The pressure was slightly increased (240 mm. H_2O), and the cellular content was 20 erythrocytes per cubic millimeter and 68 leukocytes per cubic millimeter, with a differential count of 93% lymphocytes and 7% polymorphonuclear leukocytes. Cultures of the spinal fluid remained sterile.

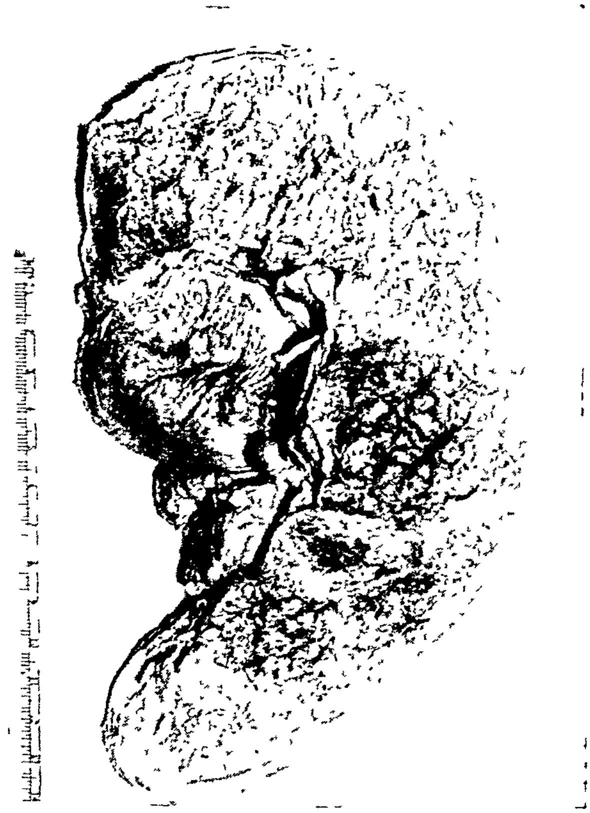

Fig. 3.—Cut surface of spleen, showing splenic infarcts.

On the third hospital day it was noted that the patient appeared to be more confused. The Kernig and Brudzinski signs were positive. He gradually became more lethargic, with intermittent periods of excitement, which were slightly relieved with morphine. On the ninth hospital day there was a right-sided hemiparesis, with Babinski and Hoffmann signs on the right. The lungs remained clear. There was now a loud systolic murmur in the aortic area. A sacral decubitus ulcer was observed at this time. Gastric tube feedings were begun. On the 12th hospital day petechiae were noted over the trunk and upper extremities (fig. 1); there was also a left subconjunctival hemorrhage. The spleen was palpable. The decubitus ulcers were becoming much larger. The urine was grossly bloody. Episodes of epistaxis developed. On the evening of the 12th day the patient became comatose. His blood pressure remained fairly stable at around 110/60 mm. Hg, with a rapid pulse rate, ranging from 120 to 150 per minute. In spite of albuminuria, which went as high as 100 mg.%, therapy with polymyxin B was resumed on the 14th hospital day.

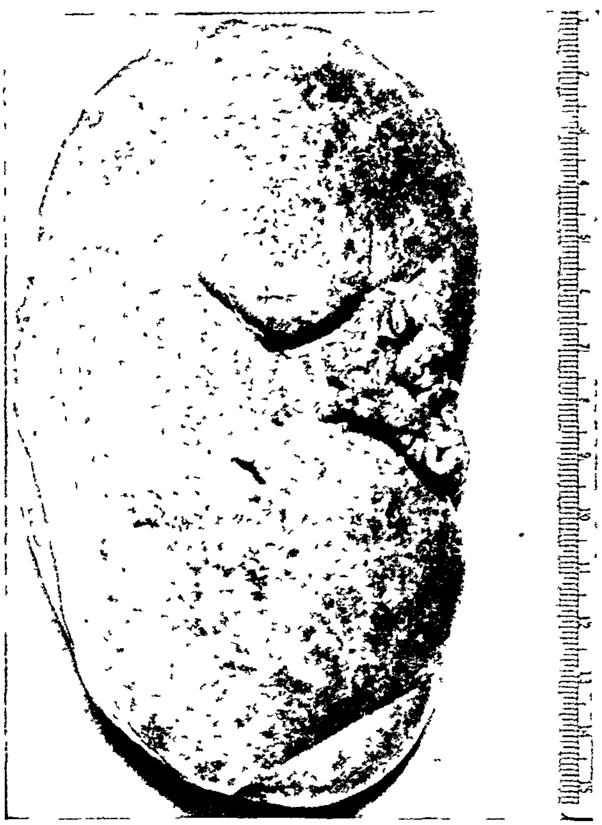

Fig. 4.—Kidney, showing petechiae.

On the 15th hospital day the patient's respirations became rapid and deep, but his lungs remained surprisingly clear. The patient died on the 17th day after admission.

Autopsy Findings

External examination revealed petechiae over the entire body, but these were most numerous over the trunk. The heart weighed 500 Gm. There was thickening of the leaflets and cusps of the mitral and aortic valves, with pale yellow-gray discoloration of the edges. Loosely adherent friable dark red-brown material was adherent to the cusps of the tricuspid and mitral valves along their lines of contact. Attached to the ventricular surface of the anterior cusp of the aortic valve was a friable vegetation measuring 4 by 3 by 2 cm. (fig. 2). Some similar tissue was present on the ventricular surface of the left posterior cusp for a distance of 1 cm. from the valve edge. There were subcommissural adhesions between all cusps of the aortic valve. Many of the chordae tendinae and papillary muscles were shortened and thickened.

The spleen weighed 1,600 Gm., and broad dull yellow-gray depressed bands were noted over its surface. Cut sections revealed numerous wedge-shaped pale gray-yellow splenic infarcts (fig. 3). The kidneys weighed 350 Gm. each. The surfaces were smooth and covered with petechiae except for several depressed pale yellow scars (fig. 4). The cut surfaces (fig. 5) showed distinct cortical striations and an abrupt corticomedullary junction. There were triangular-shaped areas of pale pink-yellow discoloration on the cut surfaces of both kidneys. Segments of the small and large intestine were discolored dark purple for distances up to 35 cm. In these areas of discoloration of the intestine there were nodular elevations measuring up to 0.8 cm. in diameter (fig. 6). The mucosa was grossly ulcerated over one of these nodules in the small intestine. The middle cerebral artery was found to have lost its usual delicate structure. It appeared to be occluded by antemortem blood clot, and there were two areas of dark red-brown softening of the left cerebral hemisphere. The larger of these was in the parietal lobe and measured 5 cm. in diameter, and the smaller was in the frontal lobe and measured 0.2 cm. in diameter.

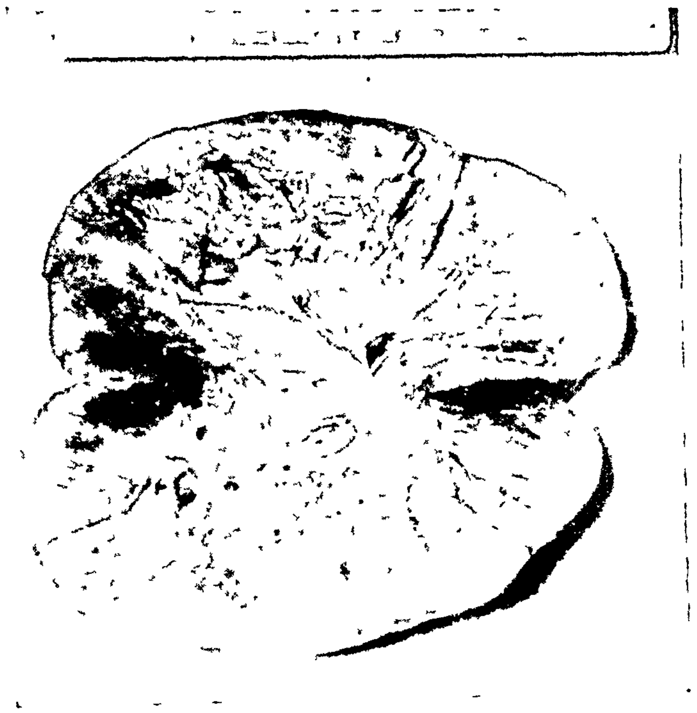

Fig. 5.—Cut surfaces of kidney, showing infarcts.

Microscopic sections of the aortic valve revealed dense, somewhat irregularly arranged fibrous connective tissue. Attached to this in one area of the section was seen a fibrin network in which were entrapped polymorphonuclear leukocytes and an occasional lymphocyte. Along the free edge of the fibrin layer and occasionally within the loosely arranged connective tissue were collections of basophilic material which under higher magnification were found to consist of basophilic rod forms of bacteria. These bacilli were not seen within any of the inflammatory cells. Sections of the coronary arteries showed infiltration of the media with segmented neutrophils and occasional clumps of basophilic rod forms of bacteria. Within the adjacent myocardium there were also many segmented neutrophils. Microscopic sections of the kidneys revealed acute glomerulitis and an occasional area of focal embolic glomerulonephritis. Also recent infarcts of the kidneys were observed. Cultures taken at autopsy from the heart blood and the aortic vegetation yielded pure growth of Ps. aeruginosa

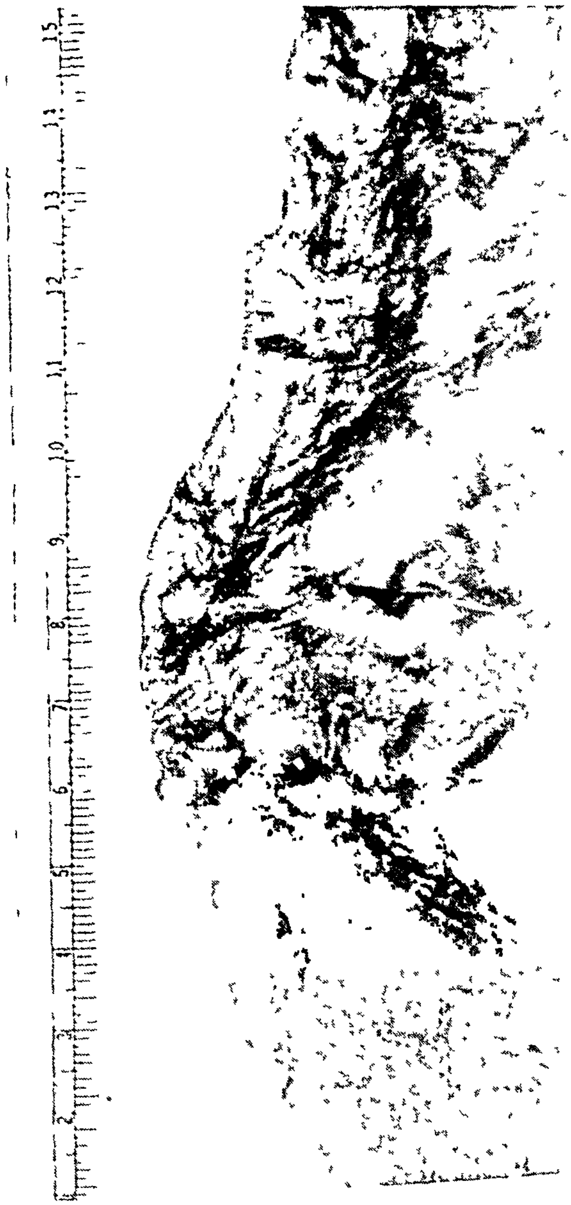

Fig 6.—Mucosal surface of segment of jejunum, showing ulcerated nodule.

The anatomic diagnoses were acute vegetative bacterial endocarditis of the aortic, mitral, and tricuspid valves, with septic infarcts of the spleen, kidneys, small and large intestine, and cerebrum; old rheumatic endocarditis of the aortic and mitral valves, and hypertrophy and dilatation of the heart

Comment

To conserve space, Ps. aeruginosa bacteremia will not be discussed except to say that more than 150 cases were found to be recorded in our search of the literature. The majority were sequels of urinary tract infections, in most of which the microorganism was introduced by instrumentation. Another important group of blood stream infections were secondary to burns. Somewhat over half of the patients reviewed died, in spite of therapy with streptomycin, polymyxin B, and tetracyclines. Good reviews of the literature on Ps. aeruginosa bacteremia appear in papers by Waisbren and Hastings[1] and Martin and co-workers.[2]

The 10 recorded cases of Ps. aeruginosa endocarditis are summarized in the table. All were fatal. It will be noted that only one other case[3] was known to be secondary to intravenous introduction of a narcotic. In only two of the nine other cases was the aortic valve the site of infected vegetations.

Reported Cases of Pseudomonas Aeruginosa Endocarditis

Author	Age, Yr	Sex	Portal of Entry	Values Involved	Previous Damage to Valves	Gram Negative Bacilli in Valvular Lesion	Damage to Other Tissues
Blum, S Centralbl Bakt 25 113, 1899	2½ mo	M	Skin	Mitral	No	Yes	Congenital syphilis, rhagades & skin eruption
De la Camp, O Charite Ann 23:92, 1903	51	F	Skin?	Mitral	None mentioned	Ps Aeruginosa isolated in pure culture	Polyarthritis; hemorrhagic diathesis
Rolly Munchen med Wchnschr 53:1390, 1906	28	F	Uterus?	Mitral	Old rheumatic	Yes	Meningitis; metastatic abscesses of spleen & kidneys
Thayer, W S Johns Hopkins Hosp Rep 22:1, 1926	42	F	Gastro intestinal tract	Mitral	None mentioned	Yes	Ulceration of small & large intestine, with perforation & peritonitis; rectovaginal fistula; pulmonary tuberculosis; pleurisy & bronchiectasis; carcinoma of stomach
Bungeler, W Frankfurt Ztschr Path 35 428, 1927	65	M	Intravenous	Mitral	Endocarditis of mitral valve 7 yr earlier	No	Ps aeruginosa, Pr vulgaris, & hemolytic streptococci in spleen
Kearns, J J[3]	35	M	Parenteral injection (probably intravenous)	Aortic & mitral	No	Yes	Abscess at puncture site
Fish, G W, and others Am J Path 13:121, 1937	71	M	Urinary tract (probable site of prostatectomy)	Aortic	No	Yes	Infarcts of kidneys
Moragues, V, and Anderson, W A D Am Int Med 19:146, 1943	66	M	Urinary tract	Mitral	Old mitral endocarditis	Yes	Diabetes meninges, arteries, spleen, lungs, kidneys, & prostate involved by gram negative bacilli
Waisbren and Hastings[1]	81	M	Urinary tract	Mitral	Yes	Yes	Subacute bacterial endocarditis extended into left atrium
Present case	23	M	Intravenous	Aortic, slight involvement of mitral & tricuspid	Old rheumatic endocarditis	Yes	Septic infarcts of spleen, kidneys, cerebrum, small & large intestine

Summary

A case of acute bacterial endocarditis was established to be due to Pseudomonas aeruginosa and is unusual in that the aortic valve was primarily involved. As in all but one of the previously established cases there was no phagocytosis of the bacilli. Involvement of the media of the coronary arteries was found; involvement of arteries was also reported in all but one of the previously established cases.

250 E. Superior St. (11) (Dr. Rhoads).

The polymyxin B used in this case was supplied as Aerosporin through the courtesy of Burroughs Wellcome & Company, Inc , of Tuckahoe, N. Y.

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CEREBROSPINAL FLUID PROTEIN AND GLYCOPROTEIN LEVELS IN CONGESTIVE HEART FAILURE

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and
Nezahat F. Henderson, M.S., Washington, D. C.

Apostol and associates[1] reported that the glycoprotein concentration in the cerebrospinal fluid (CSF) was frequently increased in neurological diseases; the level was especially high in patients with brain tumors. It was shown by Roboz and coworkers[2] that the serum glycoprotein content is also increased in cases of central nervous system neoplasms. Other workers have indicated that diabetes,[3] myocardial infarction,[4] and rheumatic diseases[5] may be associated with an increase in the serum carbohydrates which are bound to protein. In addition, this serum change has been observed in patients with congestive heart failure.[6] It seemed pertinent to determine if the glycoprotein content of the cerebrospinal fluid, as well as of the serum, was increased in a common systemic disease, such as congestive heart failure. Such information would be of importance in assessing the specificity of elevations of the CSF glycoprotein level for lesions of the nervous system and in avoiding misinterpretations of results of CSF analyses when a patient in heart failure displays neurological symptomatology. Accordingly, the CSF glycoprotein level was determined in a series of patients all of whom were in, or had recently recovered from, congestive failure.

Results of Cerebrospinal Fluid Analysis and Venous Pressure Determination in Nineteen Patients with Heart Disease

Case No.	Total Protein Level, Mg. per 100 Ml.	Total Polysaccharide Level, Mg. per 100 Ml.	Glycoprotein Level, Mg. per 100 Ml.	Mucoprotein Level, Mg. per 100 Ml.	Venous Pressure, Mm. Hg	CSF Pressure, Mm. H_2O	Heart Failure	Diagnosis*
1	47	3.1				140	—	HCVD
2	38	3.4			330	300	+	H&ASCVD
3	29	1.6	1.0	0.5	270	300	+	CHD
4	53	3.0	2.5	1.0		140	—	HCVD
5	57	3.0			300	220	+	HCVD
6	34				300	370	+	HCVD
7	27	1.0			270	350	+	HCVD
8	47	2.5			78	195	—	H&ASCVD
9	27					130	—	ASCVD
10	41	3.9			145	220	+	HCVD
11	38	2.1				300	+	ASCVD
12	38	3.3	1.8	1.3		200	+	ASCVD
13	38	1.7			260	200	+	HCVD
14	47	2.2	1.4	0.8	65	140	—	ASCVD
15	28	1.8	0.9	0.7	275	280	+	RHD
16	40	1.9				220	+	HCVD
17	38	2.0	1.0	0.9		300	+	CP
18	33	1.7				190	—	HCVD
19	40	1.8				150	—	RHD

* *HCVD* = hypertensive cardiovascular disease; RHD = rheumatic heart disease; CHD = congenital heart disease; ASCVD = arteriosclerotic cardiovascular disease; CP=cor pulmonale due to emphysema and pulmonary fibrosis.

Materials and Methods

The cerebrospinal fluid sample was obtained by lumbar puncture from 19 patients who either were in congestive failure at the time or had been in failure within the prior 14 days. The CSF pressure was recorded, and in 10 cases the venous pressure was measured simultaneously. The blood cell count was normal and the result of a serologic test for syphilis negative in each instance. The etiology of the heart disease was established on clinical grounds (see the table). Utmost care was taken to exclude patients from this study whose history or physical examination suggested a coexistent neurological disease.

The CSF protein level was determined by a modification of the biuret method described by Weichselbaum.[7] Normal values, as obtained in this laboratory, ranged from 15 to 45 mg. per 100 cc., with a mean of 35. The glycoprotein or total polysaccharide concentration was determined by alcohol precipitation of the high molecular weight carbohydrates (free and bound to protein), which were then analyzed as milligrams of hexose. The method has been described in detail elsewhere.[8] In some cases the two principal fractions of the total glycoprotein level were determined. These are, according to Winzler's classification,[9] glycoprotein and mucoprotein. The procedure used was a modification of one used for serum by Weimer and Moshin[10] and has been previously reported by Roboz and associates.[11] It is based on the fact that the mucoprotein is not precipitated by a perchloric acid solution and, thus, may be separated from the precipitated glycoprotein. The mucoprotein may then be precipitated by phosphotungstic acid and analyzed for hexose content.

The normal CSF total glycoprotein or polysaccharide content, based on that found in 15 subjects, was 1.44 ± 0.47 mg. of hexose per 100 ml. The

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glycoprotein hexose level was 0.91 ± 0.32 mg., and the mucoprotein hexose was 0.53 ± 0.12 mg. per 100 ml.

Results

The results are listed in the table. Only 3 of 19 patients had a CSF total protein level of over 50 mg. per 100 ml. Six of 17 patients had total polysaccharide levels which exceeded the normal mean plus three standard deviations. A study of the table reveals that there was no correlation between the total polysaccharide and the total protein levels. Elevations of either bore no relationship to the height of the venous or CSF pressure, the presence of congestive failure at the time of lumbar puncture, or the etiology of the heart disease.

In six patients the glycoprotein and mucoprotein hexose levels were determined. In two of these, the amount of both fractions was over three standard deviations higher than the mean, while in one patient the mucoprotein hexose level alone was elevated. The relation of the CSF pressure to the venous pressure may also be seen in the table. Every patient in congestive failure had an elevated CSF opening pressure.

Comment

The results obtained in this study of cerebrospinal fluid protein level are in agreement with those reported by Merritt and Fremont-Smith,[12] who found normal levels in the majority of the cases of congestive failure they studied.

It is difficult to quantitate the relationship of the CSF pressure to the venous pressure, since an accurate measure of the former was precluded in most cases by the inability of the dyspneic patients to lie perfectly flat in bed. An elevated CSF pressure was found only in patients who were in failure, and in these the venous pressure, when taken, was also elevated. No constant ratio between the venous and CSF pressures was observed. This is in agreement with the report of Friedfeld and Fishberg[13] but differs from the relationship noted by Harrison,[14] who calculated a ratio of CSF to venous pressure of 1:6 both in normal subjects and in patients in congestive failure.

An appreciable number of patients in congestive heart failure, or who recently recovered from failure, had an elevated CSF glycoprotein concentration. The presence of these elevations could not be correlated with any other clinical or laboratory manifestation of congestive failure. They were not associated with a coexistent neurological disease, since care had been taken to exclude such coincidences from this study. It is likely, therefore, that the increased CSF glycoprotein content in the cases of congestive heart failure reflects a systemic abnormality. Preliminary data suggest that the serum glycoprotein level is also elevated.

It may be concluded that an increased CSF glycoprotein level does not necessarily indicate a disease primarily involving the nervous system. Thus, care must be exercised in the interpretation of this abnormality when it is present in a patient with serious heart disease.

Summary

The cerebrospinal fluid (CSF) pressure and protein and glycoprotein hexose levels were determined in a series of patients all of whom were in or had recently been in congestive heart failure. The CSF pressure was elevated in those patients in congestive failure. The total protein content was usually within normal limits in all cases. In 6 of 17 cases the CSF glycoprotein level was significantly elevated. An increased CSF glycoprotein level is therefore not specific for neurological disease and should not, in itself, suggest a neurological disorder in a patient in heart failure.

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MEDICINE AT WORK

ROBBER OF FIVE MILLION BRAINS

Milton Golin

Twenty-six terrified children are riding with you this Spring as their school bus careens wildly over the steep and winding road near Ironton, Ohio—and you jump as they jump, in wide-eyed ones and twos, when the bus slows crazily at every curve. The driver is intoxicated—a problem drinker.

You stand beside the bleary-eyed executive in his locked Manhattan office while he bangs down a rubber stamp facsimile signature which, he hopes, will excuse him from the scrawl that is a dead giveaway of the shakes. Liquor is his boss.

Smell the breath of that Texas salesman as he stops his car to "fortify" himself with a swig of rum. Catch the Wisconsin logger's wife when he knocks her across the room in bourbon rage. Peek through the apartment window of the San Francisco typist "staying in with a headache" while she solitarily starts an all-day gin binge.

This is alcoholism: A complex disease that prompts the unthinking to joke about drunks but can leave families homeless and penniless; a massive medical puzzler which is no less soluble because it also is a major sociological and economic problem; a public cancer that can turn some men against themselves but to which others are completely resistant; a blight so singularly human that the Bible warns against it, Shakespeare diagnoses it, and Tennessee Williams builds a prize-winning play around it.[1]

Drink has taken 5 million men and women in the United States, taken them as masters take slaves and new acquisitions are going on at the rate of 200,000 a year. Yet, the disease that lurks in alcohol is a fickle tyrant—choosing, unexplainably, the one drinker out of every 16 over whom it is able to exert complete control. This is because, in a larger sense, the culprit is not alcohol. It is alcoholism. Oddly enough, the great majority of drinkers cannot acquire this sickness no matter how hard they may try.

One who tried is a New York City physician who, purely in the interest of medical science, set out to prove with his own body that alcohol was as addictive as morphine. He loaded the trunk of his car with cases of whisky and drove to an isolated cabin in New England. There, day after day and night after night, he drank and sang and drank. But he was not happy. For at the end of one solid month of inebriation, when this doctor returned to his office to measure his cravings and physical dependency upon alcohol as a drug, only one thing was certain: He did not want to look at liquor for the rest of his life.

What the experiment did prove (and the proof is not new) was that alcoholism, like cancer, cannot be implanted in simply anyone by physiological means alone. A multiplicity of other conditions also are disease factors. Tests with animals tend to bear this out. An elephant, for example, is subject to severe stomach cramps if it is exposed to cold weather for any great length of time and will start trumpeting with pain. Its physical hurt plus accompanying psychological stress can be relieved by a large bucket of gin and ginger. But, after taking this remedy a few times the elephant becomes a crafty alcoholic, feigning pain and moaning pitifully for his daily swig. Cats have been turned into alcoholics by spiking their milk with liquor while placing them in a variety of frustrating situations. In similar tests with rats under nonstress conditions, the rodents were able to take their whisky or leave it.

Alcoholism in man is basically a brain disease—insofar as the brain is a physiological organ subject to blood changes, a psychological organ subject to mental and emotional stresses, and a sociological organ subject to interpersonal demands and byplay.

From Torture to Treatment

Ever since prehistoric man first learned the technique of fermentation, he has been troubled with problems of intoxication and—as he became more "civilized"—of alcoholism. In those millenniums, drink toppled kingdoms while clergymen preached its evils; it betrayed armies while governors imposed stiffer penalties and crueler tortures on drunkards. Medical researchers more than a quarter of a century ago took alcoholism out of the category of moral dereliction. But only in relatively recent years have influential men and organizations come to realize that compulsive drinking is immune to punishment and sermonizing and that alcoholism is a disease which is best assailable under a compassionate and concerted attack by many segments of society. Like syphilis, alcoholism at last is being fought out in the open—spotlighted as a disease that responds to treatment, rather than beclouded as an irredeemable moral failing that forever must be condemned in the individual and tolerated in the mass.

Dr. Gunnar Gundersen, President of the American Medical Association, says: "We are under no delusions that the problem can be completely solved by purely scientific methods. The physician can restore the alcoholic's physical health, calm him mentally, and help him to meet basic human problems. At the same time, however, the ultimate solution may have to come from the patient's religious counsellor, his wife, employer, or whatever source might hold the trump card for an individual case. The medical profession is cooperating with voluntary agencies, public health groups, and legal authorities in developing a unified approach to the alcoholism problem."

Who are medicine's allies in the war against alcoholism? They are clergymen and businessmen, labor leaders and schoolteachers, lawyers and bartenders, policemen and playwrights. And they are the alcoholics themselves.

Every recovered alcoholic is a particularly incisive fighter against his own disease—more thorough than the ex-tuberculosis patient trying to limit the spread of tuberculosis, more effective than the heart attack survivor seeking to defeat cardiac diseases, more influential than the cancer victim hoping to ease the lives of others stricken like he is. More than 150,000 of these victims-turned-counsellors next year will observe the 25th anniversary of

WHAT IS AN ALCOHOLIC? WHAT IS ALCOHOLISM? SOME DEFINITIONS . . .

How do you define alcoholism? What is an alcoholic? A variety of answers are quoted here from observers who, in their diverse descriptions, not only express shadings of viewpoint but also illustrate the complexity of this disease.

"Alcoholism is a complex disease having physiological, psychological, and sociological implications." —*National Council on Alcoholism*

"Alcoholism is drinking to escape problems created by drinking."—A panelist at *Yale Center of Alcohol Studies*

"Alcoholism is reached when certain individuals stop 'bragging' about how much they can drink and begin to lie about the amount they are drinking."— A. M. A. Archives of Industrial Health

"Alcoholism is a chronic behavioral disorder manifested by repeated drinking of alcoholic beverages in excess of the dietary and social uses of the community and to an extent that interferes with the drinker's health or his social or economic functioning."

—*Mark Keller, managing editor,*
Quarterly Journal of Alcohol Studies

"Alcoholism represents the abnormal survival in adulthood of a need for the infantile normal experience of unitary pleasure of body and mind. The alcoholic rediscovers this experience in the course of intoxication. He cannot resist its gratification, however illusory or temporary it turns out to be." —*Giorgio Lolli, New York physiologist*

"One drink is too many. Twenty are not enough."—*Skid Row alcoholic in medical interview*

". . . an obsession of the mind coupled with an allergy of the body." —*Alcoholics Anonymous*

"One becomes an alcoholic when he begins to be concerned about how activities might interfere with his drinking instead of how drinking might interfere with his activities."

—*World Health Organization*

"First the man takes a drink,
Then the drink takes a drink,
Then the drink takes a man."

—*Japanese proverb*

"The alcoholic drinks because he has to. The drunkard drinks because he wants to. Once the alcoholic starts drinking he can't stop. The drunkard can stop whenever he feels like it. When the alcoholic drinks, all he can think about is where he will get his next drink. When the drunkard drinks, he wants only to get high and enjoy himself. . . . Most alcoholics start out as social drinkers. But who knows where the responsibility for his becoming an alcoholic lies?"

—*Father Ralph S. Pfau, a recovered alcoholic, in his book, "A Priest's Own Story"*

"A drinking man's someone who wants to forget he isn't still young and believing."

—*From Tennessee Williams'*
"Cat on a Hot Tin Roof"

"The drinker who uses judgment allows his body to utilize the drink he has consumed before he takes another. But the alcoholic continues to drink, unable to control his compulsion. Many an alcoholic would literally drink himself to death if nature did not intervene by causing unconsciousness. It is difficult to recognize when social drinking ceases and alcoholism begins."

—*Marvin A. Block, Chairman,*
A. M. A. Committee on Alcoholism

their savior, Alcoholics Anonymous. Their "strength amid weakness" is shown today in the successful activities of 7,000 AA groups across the nation.

Yet, because the therapy of Alcoholics Anonymous tends to help only those who can adjust to the intense group life of its program, many alcoholics are not treatable through this approach. By their very nature, most alcoholics are antisocial. A New Jersey alcoholic recently put it this way to a physician: "I don't see the point AA preaches. I don't like to hear other people's troubles." Nevertheless, Alcoholics Anonymous remains one of the effective ways of dealing with the sickness. For thousands of victims it is the avenue for a life free from compulsive drinking.

Action Across the Country

Not only in AA but in the efforts of diverse organizations and individuals all across the land this disease is being fought today with a vigor never before seen. These forces are combining with the medical profession in a tone of courage, and not plodding along separately in a panicky defeatism that "something, anything, must be done."

—In New York City, clergymen and judges are joining medical leaders as lecturers in a new course established at Fordham University for social workers dealing with alcoholics.

—In Chicago, the police department operates a Fellowship Club for the rehabilitation of officers afflicted with alcoholism. Founded in 1954, it is the first organization of its kind, and is being used as a pattern by police administrators in San Francisco and other cities. A decade ago no police force would dare admit it had an alcoholism problem.

—In Westport, Conn., a volunteer citizens committee last year began manning an alcoholism information center for that city and nine surrounding communities "to help prevent and arrest alcoholism through education in school, in the church, in the medical profession and in the community."

—In California, a 10% liquor license fee increase which went into effect last year is helping to finance eight alcoholism rehabilitation clinics on a shared-cost basis with communities.

—In Boston, officials of the General Electric Company launched its in-plant program for problem drinkers by sending the firm's personnel workers and foremen to special evening classes on alcoholism at Boston University. Problem drinkers get team treatment and group therapy at the Boston Committee on Alcoholism clinic, which is manned by psychiatrists, psychologists, family advisors, and vocational counsellors.

—In Pittsburgh, members of the Allegheny County Medical Society's committee on alcoholism work with police, judges, prosecutors, and the local bar association to help provide expert testimony when motorists are accused of driving while intoxicated. The physicians do this by operating a breath analyzing machine in the police station and appearing in court on specific cases.

—In Minneapolis, when a Foundation on Prol lem Drinking was set up recently, among those vc unteering their services (along with physicians ar social workers) were bartenders and policeme The bartenders are proving valuable in recognizin alcoholics and counselling them, and police hav learned to detect early signs of alcoholism so th these drinkers can be taken to the foundation i stead of to jail.

—In Buffalo, for the first time in the history labor-management relations, an arbitrator recent ruled on a case involving an employee fired f being an alcoholic. The decision favored the en ployee, a television announcer, on the basis of me ical testimony—and scolded the broadcasting con pany for ordering the discharge "without seekin medical advice on his condition and prognosis."

—In Birmingham, Ala., seven companies and 1 unions have joined their efforts to help alcohol workers.

—In New York, in a few weeks, a special confe ence is scheduled to frame proposals for specif alcoholism programs and services as part of offici AFL-CIO policy. Already, thousands of union cou sellors across the United States have been traine to recognize alcoholic workers and refer them t proper medical service and allied agencies.

Helping the Half-Man

Alcoholism case-finding is an even more impo tant goal of management, as it seeks to help th problem drinker before he reaches the full com pulsive stage of his illness. It is not the raucou drunk swaggering on the job who poses the bi problem for business and industry. These fellow are rare exceptions. The typical alcoholic employe or executive appears deceptively normal. But h sneaks his drinks. He douses his hair with chea perfume and may talk through the side of hi mouth in an attempt to camouflage his breath. H is a "half-man" on the job—displaying enough responsibility to prevent him from staying home, bu performing 50% or more below normal.

The medical director of one West Coast aircraft firm makes a practice of calling at the homes of workers who, possibly as problem drinkers, consistently fail to show up at the plant on Mondays. On one such visit he discovered to his amazement that a plant supervisor who happened to be his personal friend was an alcoholic. "I was completely fooled," said the doctor. "Never suspected he was a compulsive drinker. It just happened that I went to his home to see if he had been in an accident. He was pitifully drunk. Lucky I found out because now I can help."

Some companies operate their own alcoholic rehabilitation programs, complete with specialized medical facilities. Other firms band together to underwrite treatment centers. These facilities, often functioning also as a service for the entire community, include the highly effective Chicago Committee on Alcoholism (supported for the community by 300 companies), the Clinic for Alcoholism at New York University-Bellevue Medical Center, and the clinics of several dozen local committees and agencies affiliated with the National Council on Alcoholism. The NCA is an independent group that fights alcoholism as other voluntary health agencies combat cancer and heart disease.

Role of Physician

What stands out in every community battle against alcoholism is the judgment of the physician. It is he who decides when, if, and how tranquilizers, vitamins, and the abstinence-training drugs shall be used. He is medicine at work in an even larger role, however—guiding and observing, researching and coordinating, evaluating and mobilizing, sympathizing and debunking, inspiring and persuading. He is defending patients from abuse, pioneering new concepts, trying to do a job of preventive medicine. The rub is that not enough physicians are doing this. There are still many doctors who shun the problem drinker as a patient.

At the same time, however, thousands more—particularly general practitioners—are now beginning to realize that the burden of treating an alcoholic no longer need be borne by them alone—that there are growing numbers of medical and nonmedical resources available to help in the task. And where community resources are not available, some physicians are taking the initiative in organizing these facilities.

Alcoholism is, perhaps, the only major public health problem which taxes the private physician's total knowledge, wisdom, patience, skill, and compassion to the utmost—for the chronic inebriate stands alone in his challenge as a patient. Yet, by working with outside resources in helping to bring about recovery, the doctor is saving not merely a patient but a family and families to be; salvaging an integral element of the community; benefiting the lives of many people he may never know or even see. Dr. Marvin A. Block of Buffalo, Chairman of the A. M. A. Committee on Alcoholism, describes medicine's role this way:

"In the chronic alcoholic we are dealing not only with a sick individual but with that individual in relationship to his environment. There is no miracle drug that will do away with the illness. There is no known cause of this disease, no constant symptomatology, no specific treatment, no foolproof method of picking out victims in advance. An alcoholic's proneness to the disease is a secret between him and the bottle. And so the physician must not only rehabilitate his patient physically, he must help him to mature emotionally. This requires time, investigation, and patience—one does not scold a sick person. We cannot afford only to be doctors. We are also citizens. This means that it is also the responsibility of physicians to do such things as help mobilize lay forces fighting alcoholism, and inform legislatures of what they think should be done to help solve the problem. For it is a problem which ultimately affects—sociologically, psychologically, and economically—every single man, woman, and child in the United States. The physician has in the alcoholic a challenge from which he cannot retreat."

Alcohol as a Paradox

One reason that alcoholism is such a difficult disease is that its exciting agent, alcohol, is a two-faced creature—a liquid that holds both good and evil, that can provide release or can enslave. Without doubt, this mysterious and sometimes unpredictable catalyst of the brain has some therapeutic value as well as harmful effects. While alcohol is not a specific or cure for any disease, in moderate doses

DRINKING AND DRIVING

How many drinks make a person unfit to drive? The number varies with the individual, but one point appears certain: When the percentage of alcohol reaches a certain level in the blood, that person should not be behind a steering wheel. Within a few weeks THE JOURNAL will begin publishing a series of articles on this subject by outstanding, authorities in cooperation with the A. M. A. Committee on Chemical Tests for Intoxication. The chairman of that committee, Dr. Herman Heise of Milwaukee, says:

"Many people firmly believe that if they don't run into a hydrant as soon as they drive with a few drinks under their belt, and have actually negotiated long trips in spite of a load of alcohol, then alcohol does not affect their driving. The loophole in such reasoning is that no man can judge the effects of alcohol on himself when all his judgments are somewhat addled by alcohol."

Dr. Heise believes that if all drinkers—not merely alcoholics—could be divorced from driving, "possibly half of our 40,000 people doomed to die on the highways could live, and a half million more could be spared from painful and crippling injuries." His viewpoint is shared by New York Traffic Commissioner T. T. Wiley, who only a few weeks ago challenged the nation's leading electronics engineers to develop a device that would automatically stop a car if the driver were drunk.

It is in New York that records recently pointed to the possibility that we may be greatly underestimating the impact of driver intoxication upon motor vehicle deaths. These records showed that a full 55% of all motorists killed in New York City last year had been under the influence of alcohol. A similarly high proportion of traffic fatalities among drunken drivers is reported in surveys being studied by the A. M. A. Committee on Medical Aspects of Automobile Crash Injuries and Deaths.

blot out and forgive any sins if the alcoholic is only contrite and repentant. An alcoholic already is suffering truly excruciating physical and mental anguish. Portraying God as a stern, unrelenting Diety who inexorably demands His pound of flesh for each sin committed will often load down the alcoholic with what he feels is an insupportable burden that only further drinking can ease for him."

Emotional burden is inevitable as a factor in alcoholism. In fact, some researchers believe that, but for the repressions, strains, and guilt which appear to be part and parcel of our complex society, there might be no alcoholism problem at all. They point out that the disease is practically unknown in the less inhibited primitive cultures, where there may be alcoholic sprees and even extreme intoxication, but no compulsive drinking, which is the distinguishing mark of alcoholism.

The tensions and anxieties of our modern societies also are related to an increase of drinking among women in the last several decades, according to Psychologist Edith S. Lisansky, an authority on women alcoholics. But she adds that there is little evidence of any dramatic rise in the incidence of alcoholism among women. Estimates of the number of women alcoholics in the United States range from one million to two million. Only in recent years, with wider public appreciation of their problem as a disease, have many women come out of their solitary drinking to seek relief.

Dr. Lisansky believes that a mother addicted to drink produces an even greater disruption of family life than does the alcoholic father. In either case the behavior of an alcoholic parent can be so unpredictable and unintelligible to a child as to generate irrational guilt and stress in the youngster. One researcher at the Yale Center of Alcohol Studies expressed it this way: "When father is leading up to a drinking episode the children are put on their best behavior. When the drinking episode occurs, it is not surprising that the children feel that they have somehow done something to precipitate it."

Trends and the Future

Thus does such emotional interplay suggest a basis for communicability of the illness. If this is true, why not attack alcoholism through the entire family unit rather than treat only the stricken one? Evidence now shows that this is exactly what is being done on an ever-widening scale. There are several instances where therapy for the sober spouse solved the alcoholic's problem. Research is going on now to learn more about the part that husbands and wives of alcoholics play in perpetuating the drinking. Recently at Johns Hopkins Hospital, alcoholics and their wives were treated in concurrent group therapy sessions which emphasized the marriage. The aim—so far marked with gratifying success—has been to build a hopeful attitude for recovery by working things out as a family unit.

This approach is but one speck on the horizon as the new push against alcoholism gathers steam. These are other promising developments for the future:

—From a preventive standpoint, portrayal of alcoholism in public school programs is becoming increasingly realistic. The early manner of characterizing alcohol as a nightmarish devil is being replaced by a factual approach describing its limitations and effects.

—Variations of group therapy are being tried out in different parts of the nation in an effort to broaden the beneficial work of organizations like Alcoholics Anonymous. Encouraging results are reported, for example, at the Eastern Oregon State Hospital, where alcoholism patients meet regularly to take turns putting one of their number on the spot with merciless questions and arguments regarding their compulsive drinking.

—New concepts as to the causes of alcoholism are being explored and collated with research findings in an effort to find a way to prevent the disease—or, at least, to spot it in potential victims at an early age when preventive measures might be attempted. One medical researcher in the subject, Dr. Giorgio Lolli of New York City, has been examining the thesis that "alcoholism is a disorder of the love disposition" originating in childhood frustrations. Other new concepts being examined and re-examined concern nutritional, body chemical, and hormonal characteristics of the disease and its victims.

—The Center of Alcohol Studies at Yale University in a few years expects to announce results of a research project now under way to determine why some patients in the various state alcoholism clinics respond to treatment while others do not. Similar research has begun in New York as part of a $250,000 program to attack the problem of chronic alcoholism along educational, social, clinical, psychiatric, pharmacological, and other lines.

—The A. M. A. Committee on Alcoholism in September will report on progress of its 18-point program aimed at (among other things) evaluating alcoholism clinics; promoting the inclusion of alcoholism as a subject in schools of medicine, law, education, nursing, and social work; providing such instruction for physicians in postgraduate professional work; and developing a hospital cost study to prove that medical insurance companies can give full coverage for alcoholism, as is done now for other diseases. (At last report, the majority of Blue Cross plans provided some coverage for alcoholics but most of these did not have coverage equal to that for other ailments.)

—The A. M. A. Law Department, in cooperation with the Committee on Alcoholism, is considering plans to produce a survey manual which would contain summaries and analyses of state and territorial laws on alcoholism. This could inform the physician in any state of his obligations, responsibilities, and powers regarding care, treatment, and commitment of alcoholics.

—The National Council on Alcoholism is blueprinting a large-scale research program, starting with a $25,000 expenditure this year and extending to hundreds of thousands of dollars after a national fund-raising campaign is launched in a few years.

—With the encouragement of members of Congress, the National Institute of Mental Health this month was laying plans for supervising a $700,000 research program to study the physiological, psychological, and environmental factors behind alcoholism. It is the first large-scale federal effort against this disease.

—There is evidence already that, while more effective alcoholism case-finding is bringing this illness out into the open, consumption of alcoholic beverages on a per capita basis is dropping sharply. A recent Gallup poll showed that since 1945 there has been a decline of 18% in the ratio of alcoholic beverage consumers to total adult population. This indicates that in the past 12 years the beer and liquor industries "lost" 13 million customers.

These are the promises of the future—less drinking, more effective approaches to those who drink excessively, prevention, and better understanding through research. The promises have a firm foundation in a war that has physicians fighting alongside citizens in virtually every field of endeavor. "The A. M. A.'s program is one of total assault," says Dr. Gunnar Gundersen, President of the Association. "Medicine is on the firing line against alcoholism and is hauling up more and more ammunition."

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ALCOHOLISM AND COMMUNISM

Some Russians would have the world believe that alcoholism is a by-product scourge of capitalism itself and that the West has a monopoly on compulsive drinkers. But facts filtering through the Iron Curtain tell a more balanced story: Alcoholism is a world-wide disease that knows no national or political boundaries.

Last year Dr. A. A. Partnov, psychoneurologist in the Soviet Ministry of Health, announced: "No, we simply do not accept the many psychological and other theories about alcoholism advanced by some experts in Western countries. We do not believe that alcoholism is caused by some psychological or physiological or hereditary factor. It is caused by social factors. Alcoholism is a social disease. As socialism began developing in the U. S. S. R., as we did away forever with the fear of unemployment, as we gradually improved the conditions of labor and raised the level of social security—then alcoholism began to decline."

Yet, Dr. Partnov went on to add: "Of course, we still have not eliminated alcoholism. We still have far too much heavy drinking. But we have reason to believe that our approach is the correct one." He ridiculed as "almost incredible" the principle of Alcoholics Anonymous in the U. S., characterizing it as "the blind leading the blind." As Dr. Partnov spoke, however, correspondents in the satellite countries were finding that

—Alcohol consumption is up 35% in Hungary since the uprising of 1956.

—Ten-year-old and 11-year-old youngsters are tippling at vodka parties, and workers are starting off the day "full up to the top" in Czechoslovakia.

—Romanian peasants are trudging off to church on Sunday with raging hangovers and returning home to start drinking again.

—Polish families are spending more on alcohol than on any other single household item. Alcohol consumption in Poland is up 250% since 1936. (One worker explained, "Only what I drink is mine.")

Even the official Russian press reports quoted Soviet Dr. Lydia Bogdanovich as telling her countrymen that "drunkenness is causing psychic disorders, idiocy and other such ailments, and the time has come now for the formation of a mass, voluntary, good-living society."

Whether the sharp upsurge of alcohol consumption in the Red satellite countries represents a response to Communist discipline or whether it also would have occurred under a different sort of regime cannot be determined with certainty. Nor can it be stated as fact that the increased consumption is necessarily accompanied by a rise in the incidence of alcoholism. As a disease, however, alcoholism is assailable by medical men everywhere. U. S. Congressman Hays of Arkansas expressed this larger view last April when he told a Senate committee on his return from a trip to Russia:

"I find that liquor is a world problem. It is so serious in Russia with vodka and other alcoholic beverages that Mr. Khrushchev has taken notice of it himself. We hope the problem is solved there because we wish them well."

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NEW FACTS ABOUT THE HEART

IT IS becoming evident that the many great contributions to cardiology in the past have by no means exhausted the subject. Fresh discoveries have been following each other at an accelerated pace, and have caused a revolution in cardiac surgery within the past decade. Particularly surprising is the prospect of still further discoveries opened up by the recent work of Burns, Robson, and Smith.[1]

Their experiments on the heart were based on an earlier set of observations[2] made while they were endeavoring to maintain reflex activity in the spinal cords of decerebrate frogs. Several methods involving the forcing of saline solutions through the blood vessels proved unsatisfactory and led either to an early decline in reflex responsiveness of the cord or to edema of all the tissues. The method finally adopted consisted in perfusing the frog's vertebral canal through a cannula which admitted a humidified mixture of oxygen and carbon dioxide gas along with minimal amounts of Ringer's solution. This method, remarkably economical of Ringer's solution, kept the cord reflexly active for a period of hours. It was easy to make changes in the composition of the gaseous mixture. A valuable by-product of this early experiment was a simple demonstration that nitrous oxide differs sensibly from nitrogen in its effects on the cord. A brief period of anoxia caused by substituting nitrogen for oxygen caused an initial increase in reflex excitability before the onset of depression, but when a similar period of anoxia was caused by substituting nitrous oxide for the oxygen a purely depressant effect was obtained. This finding is a remarkably convincing and convenient proof that nitrous oxide is truly an anesthetic and not a mere asphyxiant.

In their subsequent experiments, Burns and his colleagues applied the above ideas to a mammalian heart with important results. After using Tyrode's solution to flush the blood out of the coronary system of the rabbit's heart it was possible to blow the Tyrode's solution out with a current of oxygen; thereafter the perfusion cannula was simply connected to a supply of a moist gaseous mixture consisting of 95% oxygen and 5% carbon dioxide. Thus oxygenated by way of its coronary vessels, the heart maintained a regular beat for periods of more than three hours while suspended in an atmosphere of warm, moist nitrogen.

The authors sketch a few of the possibilities in the new line of experimentation suggested by these findings. It will now be possible to work with isolated organs for longer periods than before without being troubled by edema; it will be possible to administer drugs under new conditions and to collect metabolic products in concentrated form by an occasional flushing-out of the vascular system with small quantities of saline solution. The gaseous perfusion of voluntary muscles in the cat has been found feasible. Better understanding of air embolism may result from further investigation of the initial resistance encountered when the gas is first insufflated into the coronaries. The possibilities are many.

The possibility of a circulation of gas instead of liquid is sufficiently amazing in connection with a cold-blooded animal like the frog, and in organs so motionless as the spinal cord; but that it should be possible also in the warm-blooded mammals like the rabbit and that it should suffice for so active an organ as the heart seemed too much to expect. But even these findings are not the only portents of new developments in cardiac physiology. Recent experiments by others indicate that much remains to be learned about the functions of the familiar "physiologist's nerve," the vagus. The comforting old teaching about the four cardiac effects of the vagus—chronotropic, dromotropic, inotropic, and bathmotropic—has long been recognized as an incomplete statement of a complicated situation, but new effects are still being reported.

Evidently the potentialities of living things have been underestimated. It is quite likely that the human heart, kidneys, liver, muscles, and brain can survive under conditions hitherto considered fantastic. This fact gives a grotesque twist to current discussions of space medicine. It has been customary to wind up such discussions by remarking that conditions on heavenly bodies other than our earth will not permit the existence of life "as we know it." But there are reasons now for believing that life can exist in various forms as we do not know it. The experiments of Burns and his colleagues, with the heart getting along so well on gas instead of blood, show that the limits of adaptability of living things have not yet been reached.

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WAR ON ALCOHOLISM

Exciting progress is being made these days against a disease that has plagued man for centuries. The disease is alcoholism, which haunts an estimated 5 million persons in the United States and is striking new victims at the rate of perhaps 200,000 a year. Significantly, the progress which began in force little more than a decade ago and which is gaining momentum day by day represents the purest fruition of traditional medical ideals. For, while it is true that some relatively new drugs are proving to be of tremendous help in the treatment of alcoholics, the most dramatic advances are taking place in the realm of medical philosophy, the principles of which are woven into a massive cooperative effort by scores of nonmedical organizations.

On page 1496 of this issue of The Journal, another Medicine At Work article tells of this new war on alcoholism as it is being waged by the medical profession in alliance with civic, religious, governmental, business, labor, educational, and other forces. These fighters have learned that such a complex problem, so prevalent and so imposing on the human race, must be attacked intensively by the best brains and efforts in a combination of fields before the hope of any single cure can be realized. So far, there is no cure for alcoholism. There is, however, ample human evidence that the compulsive drinker, totally abstaining by his own volition, can return to a normal and happy life under proper guidance embodying the basic concepts of physiology, psychology, and sociology.

Toward this goal, growing numbers of physicians in practice, in medical education, and in research are cooperating with practitioners in many other fields. Leading the way for the medical profession is the A. M. A. Committee on Alcoholism, established five years ago by the House of Delegates to study all aspects of the problem and work toward its solution. The Committee is under the Council on Mental Health.

As a result of its second major step in this field, the House two years ago enunciated a policy calling for greater hospital acceptance of alcoholics, and today more hospitals than ever before are recognizing that these sick people are as manageable as other patients. Already, increased public acceptance of alcoholism as a disease is encouraging countless alcoholics to seek medical treatment rather than to continue drowning their feelings in a morass of guilt that for centuries has grown with the primary characterization of compulsive drinking as a contemptible moral weakness.

The causes of alcoholism still are indefinable in the interplay of modern civilization's crosscurrent of environmental pushes and pulls. But at last the disease is being attacked systematically, compassionately, and tirelessly on a scale equal to the huge health problem that it really is.

ALIENS AND TUBERCULOSIS

Physicians throughout the United States may soon be asked to undertake the outpatient responsibility of treating an immigrating alien who has tuberculosis. Under a new revision in the immigration law, the husband, wife, parent, or child of an American citizen or of a resident alien may be permitted to immigrate to this country although afflicted with this disease. (Other aliens with tuberculosis are still barred from admission.)

While earlier regulations required specific hospitalization for a specified time for the tuberculous immigrant, under the new law this individual need not be hospitalized if the responsible physician determines that outpatient care is adequate.

Before receiving an immigrant visa permitting him to come to the United States, the alien must submit a statement from a state, territorial, or local health officer or from the director or a physician staff member of a hospital recognized by the United States Public Health Service as an institution for the treatment of tuberculosis. (These institutions are listed in a publication available from any local health officer.[1]) The statement must agree to supply any treatment and observation required for proper management of this disease in conformity with accepted local standards of medical practice. Any of the institutions or persons designated by USPHS as authorized to provide outpatient care may, however, delegate the treatment to the local family physician if proper care can be provided through him, but primary responsibility for conforming with the regulations still rests with those specifically named in the law. The Division of Foreign Quarantine of the USPHS will be responsible for checking on the immigrant's compliance and case requirements and may require x-ray films, clinical evaluations, and a report of final disposal.

Once again, there is reflected the need for close cooperation between the local health officer and the private physician. Here the USPHS is putting the primary responsibility for health where it belongs from the onset—in local hands. Congress has attempted to prevent unnecessary separation of families by such a law, and a physician who is called on to provide care for an alien with tuberculosis seeking admission to this country should be familiar with the letter of the regulation in order to carry out the spirit of the law.

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ORGANIZATION SECTION

SAN FRANCISCO MEETING HIGHLIGHTS EXPANDING ROLE OF MEDICINE

Pleasant weather and scenic beauty greeted the 13,218 physicians and 30,337 other registrants who signed in at San Francisco for the Annual Meeting from all 48 states, the District of Columbia, U. S. territories, and foreign nations. They and their families attended or took part in more than 600 scientific and technical presentations in San Francisco's new Plaza Exhibit Hall and Civic Auditorium, listened to research findings and medical reports from 500 physicians, watched a series of medical films and closed circuit telecasts, and joined in a variety of pre-convention activities and allied medical meetings. This was the ninth time since 1871 that the A. M. A. had met in San Francisco.

High points of the 107th Annual Meeting of the American Medical Association are summarized below. Earlier issues of The Journal carried some advance reports and resolutions as well as brief statements of officers. Future issues will contain an abstract of the proceedings, which eventually will be presented fully in pamphlet form.

The House of Delegates

The typical American physician's growing interdependence with allied health organizations, sister sciences, and the complex nonmedical world around him was illustrated June 23 through 27 in actions of the House of Delegates in San Francisco. Many of the 63 resolutions considered by the House emphasized doctor and doctor-patient relationships with such diverse groups as voluntary health agencies, Congress, the legal profession, nursing associations, federal departments, nuclear scientists, hospital administrators, and the United Mine Workers of America and other "third parties" in medical care.

As if to emphasize the profession's expanding role, the 112th President of the A. M. A., Gunnar Gundersen of LaCrosse, Wis., selected as the topic of his inaugural address, "Physicians to the World." He said: "The challenge of how to apply the science and art of medicine is formidable enough in itself. But it, too, has been further complicated by the changing backdrop on the American scene. Over the past 20 years we also have been called upon to consider a snowballing trend of social, economic and political developments affecting medicine."

Chosen President-Elect by the House of Delegates was Louis M. Orr of Orlando, Fla., a 59-year-old urologist who will take office at the Annual Meeting in Atlantic City next June. Named to succeed him as Vice-Speaker was Norman Welch of Boston. Also elected were W. Linwood Ball of Richmond, Va., as Vice-President; E. Vincent Askey of Los Angeles as Speaker (re-elected); Warren W. Furey of Chicago as Trustee; Raymond M. McKeown of Coos Bay, Ore., as Trustee (succeeding himself); and R. B. Robins of Camden, Ark., to the remaining one-year Trustee term of F. J. L. Blasingame, now Executive Vice-President of the A. M. A.

After the House adjourned, the Board of Trustees selected as their Chairman Leonard W. Larson of Bismarck, N. D. He succeeds Edwin S. Hamilton of Kankakee, whose 10 years of service on the Board and many preceding years in the House of Delegates was acclaimed in a standing vote of the House. The Trustees elected as their Vice-Chairman Julian P. Price of Florence, S. C., who will serve also as Chairman of the Executive Committee.

A high-point action of the 198-member House of Delegates was its selection of Frank H. Krusen of Rochester, Minn., as recipient of the Distinguished Service award in recognition of his outstanding achievements in the field of physical medicine and rehabilitation. Dr. Krusen is professor of physical medicine and rehabilitation at the Mayo Foundation, Chairman of the A. M. A. Council on Physical Medicine, and also Chairman of the intra-council A. M. A. Committee on Rehabilitation. Special lay citations for distinguished service were voted to Mrs. Charles W. Sewell of Otterbein, Ind. (the first woman to be so honored) for her pioneering efforts to improve rural health, and to Gobind Behari Lal, Ph.D., Pulitzer prize-winning science editor emeritus of the Hearst newspapers.

Prompt Action on UMWA

The House discussed an educational campaign concerning the United Mine Workers of America Welfare and Retirement Fund, which is used to operate 10 hospitals and pay physicians. The House in its action appeared to support the contention that 250,000 miners and their families—a total of more than one million people in over half the states of the nation—are not freely permitted the basic American right of choosing their own physician. At the A. M. A. Clinical Meeting last December, the House adopted a resolution calling for action to acquaint these beneficiaries as well as the general public with the charge that the Fund's operation would tend to lower the quality and availability of medical and hospital care to the miners and their families. The resolution condemned "the current attitude and operation" of the Fund. In San Francisco last month, a House reference committee again considered the situation. It then seconded a suggestion that the matter be allowed further study until next December's Clinical Meeting, when the A. M. A. Commission on Medical Care Plans would present final recommendations covering third parties in general. It was with this suggestion that the House on June 26, by a vote of 110 to 72, disagreed. It passed one resolution sanctioning postponement of action, but also voted to launch an educational campaign at once.

Aging, Indigent, and Hospitals

The UMWA controversy was aired before the heavily attended House reference committee on insurance and medical service. As a result of other matters discussed before this committee, the House:

–Recommended approval of "Suggested Guides for the Organization and Operation of Medical Society Committees on Aging," as submitted by the Council on Medical Service.

–Adopted a resolution stating that Americans have such "basic medical rights" as choosing their own physician and knowing that these individual doctors carry sole responsibility for decisions regarding the extent of medical care rendered.

–Directed the Board of Trustees to implement a resolution calling for a study "to determine whether or not the growing practice by hospitals of encouraging staff members to conduct private office practice within or adjacent to the hospital is a major move toward the practice of medicine by hospitals."

–Voted that "the American Medical Association request that any funds provided under the Public Assistance provisions of the Social Security Act for medical care of the indigent be administered by a voluntary agency such as Blue Cross on a cost plus basis or by a specific agency established by the medical society of the state in which indigent care is rendered."

The House also directed the Board of Trustees to implement a resolution which "suggests the selection of a specially designated committee to study, anticipate, educate, and in the best interests of the people prepare for future legislation relating to indigent care."

Voluntary Health Agencies

Probably the most debated issue of the meeting stemmed from three resolutions urging that the A. M. A. reaffirm its support of voluntary health agencies. After two hours of hearings, a reference committee submitted a substitute resolution which indeed praised these agencies but added the following recommendation:

> That the Board of Trustees be requested to arrange a top-level conference with the voluntary health agencies, the United Funds, the American Medical Research Foundation and other parties interested in the raising of funds for health causes, with the view of resolving . . . serious problems concerned with the raising and distribution of funds since the development of the concept of united community effort.

However, a half-dozen delegates spoke against this part of the reference committee report. Fear was expressed of the United Funds exerting lay control over huge health funds which could be administered with greater wisdom and balance by medical men. As a result of the floor discussions, the House adopted, by standing vote, a four-point substitute amendment which commended the principal voluntary health agencies, urged that they be "free to conduct" their own programs, asked that the American Medical Research Foundation "take no action which would endanger the constructive activities" of these agencies, and recommended that the Board of Trustees continue active study "of these perplexing problems."

Social Security Coverage

In considering seven resolutions dealing with the inclusion of self-employed physicians under the Social Security Act, the House disapproved of three which called for polls or a referendum of the A. M. A. membership, two which favored compulsory inclusion, and one which called for optional participation by doctors on a state-by-state basis. Instead, the House of Delegates adopted a resolution which reaffirmed unequivocal opposition to the compulsory inclusion of self-employed physicians in the Social Security system and stated that "American physicians always have stood on the principle of security through personal initiative." At the same time, the House recommended that American physicians "heartily make known to the members of Congress their support of the Jenkins-Keogh bills," which permit self-employed persons to establish their own retirement programs with proper tax deferments similar to those already granted to employed individuals. If there is to be a survey of opinion on whether doctors should be included under compulsory Social Security coverage, the House noted, such a poll should be on a state-by-state basis and the results transmitted to the A. M. A. Delegates from the respective states.

Washington Office

Citing a need "for effective liaison between government and medicine on all matters affecting the public's health," the House adopted a resolution calling on the Board of Trustees "immediately to survey and evaluate the functions and effectiveness of the over-all A. M. A. legislative system including the *Washington office.*" *The House expressed the opinion that "a redefining of the respective duties of the Washington office and the Chicago headquarters is indicated, and that because of the importance of this activity, the time to do this is now."*

In another move calling for *early action*, the House directed the Board of Trustees to explore the desirability of establishing "an entirely new special division" which would plan and execute a long range program to preserve unfettered medical practice, meet the medical needs of Americans under the voluntary free enterprise system, and "offer positive advice and assistance to state and local societies" when specific threats to voluntary medical care arise in their areas.

Other House Actions

The House also:

–Directed that a Committee on Atomic Medicine and Ionizing Radiation be appointed by the Board of Trustees to educate medical students and physicians, recommend policies on the use of radioactive material, consider appropriate legislative action, and inform "the American people from time to time on all phases of radiation hazards."

–Reiterated an earlier stand by urging congressional action to restrict bed care at Veterans Administration hospitals to veterans having service-connected disabilities.

–Approved in principle and recommended favorable action toward the admission of the Virgin Islands Medical Society as a constituent society of the A. M. A.

–Expressed the opinion that desired changes in the Medicare program could be accomplished through modification of existing directives without the need for new legislation.

–Approved a Council on Mental Health report on "Medical Use of Hypnosis" and recommended that it be published in THE JOURNAL. The report urged physicians and dentists to take part in high level research on hypnosis, and it condemned the use of hypnosis for entertainment purposes.

–Recommended that the A. M. A. join with other interested groups in setting up an expanded voluntary program to eliminate objectionable advertising of over-the-counter medicines. The program would be coordinated by the National Better Business Bureau.

–Approved a National Interprofessional Code of physicians and attorneys, prepared by a joint liaison committee of the A. M. A. and the American Bar Association.

–Urged that the Board of Trustees appoint a special committee to "develop a classification of, and terminology for, operating room deaths." The House approved a resolution noting that operating room mortality "appears to be an increasing hazard in the conduct of surgical practice" and that lack of uniformity in the compilation of operating room mortality statistics "does not permit accurate assay of the problem or comparison of these mortality statistics from different areas."

–Expressed the opinion that some operating experience is valuable and necessary training for all nurses, and recommended that the A. M. A. work with nursing, hospital, and other groups to improve the quality and quantity of nurse training.

–Asked the A. M. A. representatives on the Joint Commission on Accreditation of Hospitals to oppose the requirement of board certification as the sole qualification for staff appointments in hospitals approved by the Commission.

–Directed the Board of Trustees to consult with the Federation of State Medical Boards in an attempt to solve problems pertaining to licensure by reciprocity.

–Recommended that general hospitals, wherever feasible, be encouraged to permit the hospitalization of suitable psychiatric patients.

Other New Officers, Plaudits

Elected to standing committees of the House were George A. Woodhouse of Pleasant Hill, Ohio, to a second term on the Judicial Council; Leland S. McKittrick of Brookline, Mass. (to a second term) and John V. Bowers of Madison, Wis., to the Council on Medical Education and Hospitals; R. B. Chrisman Jr. of Coral Gables, Fla., and John F. Burton of Oklahoma City, Okla. (to second terms) and Russell B. Roth of Erie, Pa. (to fill a vacancy) to the Council on Medical Service; and William Stovall of Madison, Wis., William Hyland of Grand Rapids, Mich., and Walter Bornemeier of Chicago to the Council on Constitution and Bylaws.

The House gave a rising vote of appreciation to George F. Lull, who retired as A. M. A. Secretary, and J. J. Moore, retiring Treasurer. Dr. Lull, now Assistant to the A. M. A. President and President of the American Medical Education Foundation, accepted a record-breaking state association contribution of $177,500 for the Foundation from the Illinois State Medical Society. Earlier, the House adopted amendments to the Constitution and Bylaws which combined the separate offices of Secretary and Treasurer, and changed the titles of General Manager and Assistant General Manager to Executive Vice-President and Assistant Executive Vice-President.

In addition to bestowing honors for distinguished service, the House honored Virgil P. Sydenstricker, professor emeritus of medicine at the Medical College of Georgia, as recipient of the Goldberger award in clinical nutrition. The award consists of an engraved gold medal and $1,000. Among other awards made in connection with the meeting were the Passano Foundation award for clinical medicine research, to Dr. George W. Corner of the Rockefeller Institute for Medical Research, and medals for outstanding exhibits at the Civic Auditorium.

The House has designated future meetings as follows: The 1958 Clinical Meeting in Minneapolis, 1959 Annual Meeting in Atlantic City, 1959 Clinical in Dallas, 1960 Annual in Miami Beach (replacing Chicago), and 1961 Annual in New York City. Action was postponed on selection of a city for the 1962 Annual Meeting.

Concurrent Activities

In other activities just prior to and during convention week:

–Mrs. E. Arthur Underwood of Vancouver, Wash., took office as new president of the Women's Auxiliary. Mrs. Frank Gastineau of Indianapolis was named president-elect.

–A three-day program dealing with medical preparedness for disaster featured discussions by the four surgeons general of the U. S., a test exercise, and a statement by U. S. Congressman R. Walter Riehlman of New York that he was introducing a bill to provide tax relief for builders of properly designed bomb shelters.

–Some 400 doctors displayed their works at the 21st annual exhibit of the American Physicians Art Association.

–A half-dozen American physicians reported at a meeting of the United States Committee of the World Medical Association on the topic, "Correlated Team Work of Physician Specialists in Volunteer Medical Mission Projects Throughout Asia and Africa."

–Nineteen medical experts took part in a forum on traffic accidents as a major health problem.

–A. M. A. Councils and Committees met to discuss scores of agenda items including nursing homes, chiropractic, occupational health programs, foreign medical graduates in the U. S., insurance and prepayment plans, medical school accreditation, problems in atomic medicine, foods and nutrition, research, and rural health.

THE 1958 SCIENTIFIC ASSEMBLY

Most of the papers offered during the meeting will be published in The Journal and in the A. M. A. specialty journals during the next several months. Limitations of space prevent a summary of all the papers and scientific exhibits presented at the meeting, but some attracted special attention. When the 300 exhibitors, representing pharmaceutical houses, medical equipment firms, manufacturers, and purveyors of various medical materials and services are added to make up the total program, almost 1,000 different events were available to the more than 13,000 physicians who attended the scientific assembly.

The Physician's Attitude

The underlying theme throughout the scientific assembly might best be summarized by referring to the Section on Allergy's panel discussion on asthma. Here Dr. M. Coleman Harris of San Francisco stressed that if the attitude of the physician is one of hesitancy, uncertainty, helplessness, and lack of decisiveness in applying proper therapeutic measures, he will transmit this attitude to the patient. The seriously ill asthmatic patient, to use just one type of illness as an example, is already frightened, fearful, and anxious. If the attending physician does not instill confidence along with medicaments, the patient's anxiety will be further increased, thus aggravating the severity of the original illness. In the vast majority of cases, the doctor of today can quite honestly reassure and convince his patient that he is soon going to be relieved of his symptoms and be up and about again. The 1958 convention in itself offered the physician a tremendous armamentarium of relief-giving measures, and each new drug or technique provides another step in confidence-giving to the physician which will eventually be transmitted to his patients.

General Scientific Meetings

In the first day of the general scientific meetings, Dr. Carl A. Lincke, Carrollton, Ohio, presided over a panel discussion on the management of the severely injured patient. All the speakers emphasized the early recognition and management of the unsuspected lesion; the one which may make the difference between life and death, or between just recovery and independence. With an injured person the most important immediate problem is in recognizing the need for, and establishing, an adequate airway; preventing further hemorrhage; replacing lost blood; and, avoiding additional damage by injudicious movement of the patient or his injuries. Dr. Otto E. Aufranc of Boston felt the arrest of hemorrhage deserved specific mention. In most cases hemorrhage might be better controlled by the use of a hemostat. However, the blind application of a hemostat to bleeding vessels is to be condemned. Clamping in a sea of blood may very well destroy arterial tissue that might not otherwise be destroyed, and may preclude an otherwise repairable suture in a major vessel.

Most patients who are severely injured will have some manifestation of pain, commented Dr. Robert A. Hingson of Cleveland. Pain in itself is both defensive and protective, as well as being indicative of proper diagnosis. Once the message of pain has been understood, and the patient properly safeguarded, there is much the physician-anesthesiologist can do to remove pain, treat shock, and prepare the patient for surgery. Accident victims, especially when numerous, must be prepared in proper sequence for surgical restoration and mobilization for transport to receiving centers. Anesthesia is the first prerequisite for surgery. Dr. Hingson warned that every patient who has had a transient loss of consciousness should be observed for 12 to 24 hours after injury to make sure there is no bleeding inside the skull. This is especially true if there has been an intake of alcohol.

Dr. E. Stanley Crawford, Houston, told of over 1,400 cases of grave chest injury (e. g., gunshot and stab wounds and accidents) where the mortality rate of those given treatment was only 7.3%.

During the second general scientific session, a panel, moderated by Dr. Wesley W. Spink, Rochester, Minn., discussed adverse reactions to therapeutic agents. Antibiotics, steroids, and tranquilizers, while having helped many people, have also created medical problems, according to Dr. Harold O. Perry, also of Rochester, Minn. One of the commonest adverse reactions encountered during drug administration is skin eruption. In finding the cause of a skin reaction it may be necessary to rely heavily on the historical sequence of events. The proof of a true hypersensitivity to a drug, as determined by skin testing, may be lacking, and to duplicate the experience by introducing the suspected drug is fraught with dangers. One may be well satisfied with the partial proof of the historical evidence alone.

Dr. Laurence H. Kyle, Washington, D. C., said the introduction of steroid agents, while a major advance, has raised the problems of complications which appear in most patients who are given the drugs in large doses or for prolonged periods of time. Among the major problems resulting from steroid therapy are salt retention, potassium depletion, undesirable central nervous system effects, and tissue breakdown. The most worrisome problem is that the adrenal glands will cease to function normally during drug administration. Then if a severe illness occurs, there will be insufficient adrenal hormone available to help the patient survive.

It seems that there are many drugs that, while curing anxiety in the patient, create anxiety in the physician. Drugs may produce many complications, but their benefits in carefully selected patients outweigh the dangers, said Dr. Leo E. Hollister, Palo Alto, Calif.

General Practice Sessions

The Chairman of the A. M. A. Section on General Practice, Dr. Charles E. McArthur, Olympia, Wash., analyzed the 6,000 heart and chest examinations given doctors attending the past three A. M. A. meetings. He concluded that (1) doctors are a pretty sick group, (2) they are nervous, tense, and worry excessively, (3) they get insufficient exercise along with inadequate or incorrect diets, and (4) they have a higher annual death rate than the rest of the population.

Eighteen per cent of electrocardiograms and chest photofluorograms (there were around 3,000 of each) showed abnormalities including tuberculosis and chest neoplasms. Dr. McArthur felt that nervous tension is doubtless an occupational hazard of the medical profession that must be compensated by taking adequate vacations to cope with the problem of inadequate exercise. One suggestion he made was that, while making hospital rounds, doctors walk upstairs instead of riding the elevator. Lastly, he stressed the need for regular physical examinations—for the physician.

In other papers presented at the Section on General Practice, Drs. John H. Moyer and John R. Beam of Philadelphia discussed the pharmacology of chlorothiazide, an orally effective diuretic agent with a major action on sodium and chloride excretion, and a lesser effect on potassium and bicarbonate excretion. The onset of action is within two hours after oral administration, and the drug effect lasts approximately 6 to 12 hours. Dr. Edward D. Freis, Washington, D. C., found that this nonmercurial diuretic alone, in a dose of 500 mg. twice daily, reduced blood pressure moderately in hypertensive patients. Excessive salt intake, however, resulted in a partial restoration of the blood pressure toward pretreatment levels, suggesting that the mechanism of action of this drug is connected in some way with loss of body stores of salt. The drug has also been used successfully, and often with outstanding results in the management of congestive heart failure, according to Dr. John W. Keyes of Detroit.

Drs. Lester Morrison and Theodore L. Clemens discussed diet as the best weapon for the treatment of atherosclerosis. In addition to President Eisenhower whose underlying disease is believed to be atherosclerosis, six other presidents have died of this condition during this century. In reporting on 10 years treatment of 100 patients with coronary atherosclerosis, Drs. Morrison and Clemens feel that while this disease, the leading cause of death in the United States, appears to arise from a combination of hereditary susceptibility, being male, stress, and diet, it is diet that is the easiest factor to alter. After 10 years, 16 patients of the original controlled 50 treated by low-fat diet were still alive. During the same 10 years, all of the other 50 patients, on unrestricted diets, are now dead.

Various Section Meetings

Drs. Ellard M. and Martha D. Yow discussed hospital acquired staphylococcic infections at the Section on Internal Medicine. The management of these particular infections differ from those developing in patients outside a medically influenced environment in that they are likely to be due to strains of bacteria resistant to the commonly used antibiotics. Penicillin, streptomycin, and tetracycline are rarely active against the hospital strains of infection. Mild to moderately severe infections should be treated with novobiocin, chloramphenicol, ristocetin, erythomycin, or oleandomycin. Severe infections require such actively bactericidal agents as kanamycin, vancomycin, or bacitracin.

Of course, the widespread publicity given to the possible harmful effects of x-ray came under discussion in many of the section meetings. Drs. J. E. Miller and Gerald Swindell of Dallas, Texas, at the Section on Obstetrics and Gynecology, felt this publicity has led to an abnormal state of apprehension in the general public, due, in great measure, to the irresponsibility of the public press. By irresponsibility it was stated that the press has steadfastly refused to give both sides of the question since the common sense side does not make news. It is the physician's responsibility, and indeed his prerogative, to use judgment in the application of any hazardous medical procedure to the human being. The potentiality of irradiation causing damage to future generations should not prevent the real benefit that is obtained by using irradiation in the present generation.

Continuing with the subject of radiation, Dr. Wendell G. Scott, St. Louis, Chairman of the Section on Radiology, told of the many ways of reducing gonadal doses of diagnostic x-ray exposures. The guiding directive, Dr. Scott said, is to scrutinize each examination beforehand as to how that particular exposure can be reduced. Some suggestions: limit fluoroscopy to specific medical purposes, especially in children and infants (one minute of continuous fluoroscopy is equal to 500 chest x-ray films in total radiation exposure); have a radiation physicist survey your equipment for "leakage," out-of-date equipment, and adequacy of radiation barriers; place the x-ray tube the longest practical distance from the patient (increased distance produces less exposure); be sure the x-ray "beam" is limited to just that part of the body under study, using rectangular shutters; switch to new, fast x-ray film and high-speed intensifying screens; and be sure to develop the x-ray films in newer chemicals with full-time temperature and control. For children, lead rubber snap-on diapers were recommended; and for all persons, try to avoid repeat studies by preserving each film and its report. Once again the physician was told he must have and display an attitude of confidence in his entire diagnostic and therapeutic battery.

In the Section on Physical Medicine, Dr. Miland E. Knapp, Chairman from Minneapolis, discussed the recent changes in the attitude of the profession toward the hemiplegic patient—from one of hopelessness and rejection to one of optimism and enthusiasm—all because of advanced rehabilitation techniques. Attention is now paid, not only to the disabled area and crippling disease but also to the portions of the body that remain functional and from which the patient can carry out reasonably normal activities, not only in living but in enjoying life. In telling how brain damage is the factor limiting recovery, Dr. Knapp pointed out how right hemiplegics manifest speech and language defects but are more frequently returned to work. Left hemiplegics exhibit visuospatial defects which militate against return to competitive employment. By use of early and persistent treatment for the physical disability and by employing ingenuity and imagination in the choice of assistive devices, the great majority of hemiplegic patients can be made self-sufficient, thus relieving their family and friends from the burden of their care.

In his chairman's address to the Section on Preventive Medicine, Dr. Bruce Underwood, Washington, D. C., in a paper read by Dr. Joseph Bistowish, Tallahassee, urged that the A. M. A. take a much greater interest in physicians who are not in private practice. The need was stressed for a closer relationship between public health and clinical practice. After all, even though the practice of public health is as different from the practice of clinical medicine as all the other specialties differ from one another, public health physicians still consider themselves to be doctors of medicine foremost. Dr. Underwood made a plea that those interested in this problem communicate with the A. M. A. committee now considering the total situation.

For the first time "open heart" surgery was performed while the patient was hypnotized. In addressing the Section on Pediatrics, Dr. Milton J. Marmer, Beverly Hills, Calif., reported on two operations on teen-agers in which hypnosis was used as an adjunct to anesthesia. Dr. Marmer felt the most remarkable postoperative aspect of his cases was the absence of the complaint of pain. In children, the achievement of relaxation by means of hypnosis is worthwhile. Most doctors will be surprised at the comparative ease of inducing hypnosis in children, especially those between the ages of 7 and 14.

In speaking to the Section on Gastroenterology and Proctology, Drs. Howard F. Raskin, Joseph B. Kirsner, and Walter L. Palmer, Chicago, told how exfoliative cytology is far more accurate than x-ray in diagnosing cancer of the gastrointestinal tract. The study of cells sloughed from the organ wall is 95% accurate in diagnosing cancer of the esophagus, stomach, and colon, and 60% accurate in cancer of the pancreas and biliary ducts.

Dr. Gilbert Baum, Port Chester, N. Y., reported to the Association for Research in Ophthalmology on recent experiments proving the feasibility of visualizing the interior of the light opaque eye and the contents of the orbit by using pulsed ultrasonic echo methods. In discussing the application of ultrasonic locating techniques to ophthalmology, Dr. Baum told how the lens of the eye possesses the highest coefficient of absorption of any tissue in the eye, probably related to its high protein content. Proper interpretation of echograms necessitates a thorough comprehension of the acoustic parameters of all areas of the eye.

One way to study a man's personality is to lock him up in a dark, soundproofed room and find out what happens. Isolation is a unique tool for the study of personality and of the needs people have for environment. Space flights may be expected to disrupt normal patterns of sensory input by entailing extreme degrees of aloneness and confinement. Drs. Edwin Z. Levy, G. E. Duff, and V. H. Thaler, Dayton, Ohio, told the Section on Military Medicine of numerous reports indicating that actual and experimental sensory deprivation and isolation are highly stressful. In some cases there was a fairly rapid onset of distorted perceptions and impaired intellectual functions. Most subjects do not care and do not think while isolated, and the longer the isolation lasts the more unbearable it becomes. Schizophrenic individuals who are isolated are likely to break down in two hours, but passive dependent types do not seem to mind the effects of solitary "imprisonment." If the length of the experiment is made known to the subject in advance, he seems to better tolerate his isolation.

A paper given at the Section on Orthopedic Surgery reported that whiplash injuries to the spine are rapidly taking their place among the leading causes for litigation. Dr. Charles J. Frankel, Charlottesville, Va., made a plea for more accurate diagnosis, a more correct method of terminology, and a nonpartisan attitude on the part of physicians who examine these unfortunate patients. Any medical or pseudoscientific report which flatly infers that 80% of people who suffer injuries to the neck in automobile accidents are malingerers, should be reexamined closely, and if the facts do not bear out such a conclusion, an apology or explanation should be made. Again and again, the physician's attitude is the all-important factor.

Fully 90% of all strictures affecting the extrahepatic biliary system are man made, said Drs. N. Frederick Hicken and A. James McAllister of Salt Lake City to the Section on Surgery. It is the surgeon and his traumatizing procedures which result in the undesirable complications. Failure to recognize anatomic variations of the bile ducts, the occurrence of unexpected hemorrhages, the misapplication of crushing clamps, the improper placement of sutures, the rough instrumentation of the bile ducts, perforation of the ducts by probes, and improper closure of the choledochotomy accounts for the majority of injuries.

The Section on Pathology and Physiology heard from Dr. William Dock, Brooklyn, N. Y. Dr. Dock, in telling why men's coronaries are so sclerotic, said that lipid deposition in the coronaries begins in sucklings, and in all vertebrates but in man it disappears on weaning. In most parts of the human race this is true, but in prosperous people it progresses throughout life. The peak rate of deposition occurs in males aged 15 to 30 years. The peculiar structure of the coronary intima is more striking in males than females, even at birth, and this might explain why fatal coronary disease occurs in males under 35 with no other atherosclerotic lesion. Androgens influence the blood lipid pattern, and further accentuate male coronary atherosclerosis.

Color Television

Consideration of the pros and cons of tonsillectomy was one of the many programs presented over closed circuit color television. In a panel discussion, moderated by Dr. Robert Alway of San Francisco, Drs. Harold K. Faber, San Francisco, and Esther B. Clark, Palo Alto, Calif., felt that the lowly tonsil and adenoid may prove to be the child's best friends, helping to guard him against infection, increasing his immunity, assisting him in the creation of antibodies, and possibly protecting him against poliomyelitis. Dr. Frank Sooy of San Francisco and Dr. Alden H. Miller of Los Angeles agreed that tonsils and adenoids should not be removed except for good and sufficient cause. They felt, however, that acutely diseased tonsils and adenoids that resist modern nonoperative therapy, recurrent bouts of sinusitis, breathing obstructions, and certain types of hearing defects, were sufficient reason for tonsillectomy and adenoidectomy. While disagreement as to tonsil surgery was strictly academic, the point was made that medical knowledge will probably never stand still, and the tonsil controversy well emphasized that fact. An interesting side light was that all four panel members admitted to being without their own tonsils.

Scientific Exhibits

Throughout the scientific exhibits, specialists in all fields of medicine impart their knowledge directly to their colleagues. The physician-observer of the scientific exhibit is really a participant in a two-way learning process. He not only sees medical information in action, but in many instances actually enters into, through the sense of touch, this unique form of postgraduate education.

The endocrines and the liver in lipid mobilization was the subject of an exhibit by Drs. Joseph Seifter, David H. Baeder, and Chris J. D. Zarafonetis of Philadelphia. They showed how various forms of stress call on the body to supply calories, including those from fat stores. The most readily available fat depots are the mesenteric and omental fat beds. It is believed that stress (including exposure to cold, surgical procedures, intoxication with some chemicals, some infections, pregnancy, and experimental disease-nephrosis) stimulates the anterior pituitary to discharge ACTH. ACTH stimulates the adrenal cortex to discharge glucocorticoids; the corticoids stimulating the posterior pituitary to release LM (the lipid mobilizer substance). LM acts on the fat beds to release neutral fats into the portal circulation. If the liver is capable of handling this sudden fat load, blood leaving the liver through the hepatic veins is not hyperlipemic. Should the liver not be capable of handling this fat load, neutral fat is discharged into the peripheral circulation in association with cholesterol and lipid phosphorus, resulting in a generalized hyperlipemia. This exhibit should certainly make the physician think of hyperlipemia as a possible result of excessive or prolonged cortisone therapy.

An exhibit on intrasynovial steroid therapy by Dr. Joseph L. Hollander, Philadelphia, and his associates, stressed the most important aspect in achieving successful results with these injections is knowing the proper technique. There is a "trick" to it. Dr. Hollander demonstrated this "trick" to physicians and then let them practice under his direction. To avoid failure, the physician must know the exact anatomy of the joint involved Since publication of his first paper on this subject in The Journal back in 1951, he has found there have been failures in about 54% of the cases. But he blames two-thirds of these failures on poor technique. With proper procedures, intrasynovial therapy with hydrocortisone or prednisolone esters will result in at least temporary palliation of symptoms and signs in more than 75% of those persons where such treatment is indicated (e. g., arthritis, bursitis, tenosynovitis, tennis elbow, and diffuse collagen diseases). Relief should last from a few days to many months.

Dr. Russell S. Fisher, Baltimore, and his colleagues used a scientific exhibit to demonstrate that in the medicolegal autopsy there are certain aspects that require more attention than is usually given to an autopsy performed in hospital practice. These are clothing (patterned soiling, body fluids, trace evidence); skin and mucous membranes (petechiae, thermal and electrical burns, needle marks); subcutaneous and muscle tissue (hemorrhages, abscesses, edema); oropharynx, larynx and hyoid bone (foreign bodies, tumors, edema, injuries); middle ears (suppurative otitis media in infants); cervical vertebrae and spinal cord (poliomyelitis, cervical cord injuries); vascular system (pulmonary and carotid arteries, also lower leg veins); and chemical injury (alcohol, barbiturates, and carbon monoxide poisoning). The autopsy should be performed in such a manner that if a satisfactory cause of death cannot be identified, blood, urine, and tissues are preserved for microscopic, toxicological, and bacteriological examination. Dr. Fisher went on to say that there is no question that a substantial number of murders are missed because of failure of the physician who signs the death certificate to ever think of foul play.

In an exhibit pointing out the important surgical principles in the case of so-called minor hand injuries, Dr. Adrian E. Flatt, Iowa City, demonstrated that no hand injury can be treated correctly until the answers to the following questions have been applied to each individual wound. 1. What is the cut-crush ratio? (The neat incision heals more rapidly and the pathology differs in each case, e. g., edema.) 2. Is the wound tidy or untidy? (This does not mean "dirty"—a wound can be tidy and still dirty.) 3. Is there any skin loss? 4. Are the tendons injured? 5. Are the bones and joints involved? 6. Is the neurovascular bundle injured? 7. What is the patient's occupation? The last is probably the most important of all the questions since the entire mode of treatment depends on the job the hand eventually must do.

Dr. Max D. Moody and his colleagues from the Public Health Service Communicable Disease Center, Atlanta, displayed fluorescent antibody methods as a means of rapid diagnosis. It is hoped this staining of pathogens technique will soon be in every physician's office. The doctor can then verify his diagnostic suspicions, especially in the case of communicable disease, by selecting the proper reagents and observing immunohistochemical staining within a few hours (e. g., one could differentiate between a streptococcic throat infection, a virus infection, or diphtheria almost immediately). Fluorescent antibody reagents and high intensity lamps specifically designed for micro-organism fluorescence work are already available from commercial sources.

The key to the management of gout is prophylaxis, according to Drs. John H. Talbott and Donald Wilson of Buffalo. The most important preventive measure in avoiding recurring attacks is the removal of excess uric acid by the daily use of a uricosuric agent, plus the daily use of colchicine, the oldest antigout drug in the pharmacopeia. Diet is much less important than previously supposed, but a high fluid intake may help to carry away uric acid.

Three of the many scientific exhibits on hypertension deserve comment. One, presented by Dr. Richard F. Tislow and his associates from Radnor, Pa., introduced trimethidinium methosulfate. The drug is a new approach to hypertension because it acts by ganglionic blockade, and in addition, probably by a central component of action. Dr. Richard A. Dunsmore, Philadelphia, reporting on clinical experience with this drug, emphasized the low incidence of constipation along with its effectiveness. He felt that, while the drug was not adaptable to every hypertensive patient, it may well prove of unusual value for the severe hypertensive patient, whose condition is poorly controlled by milder agents. Dr. Burton M. Cohen, Elizabeth, N. J., stressed that the physician must document hypertension by thorough history taking, including the family history of hypertensive disease. Because separation of "poor risk" from "good risk" hypertensive patients is not possible at the moment of initial diagnosis, every patient with documented primary hypertension deserves medical therapy. Continuing with the medical therapy of hypertension, Dr. Marvin Moser, White Plains, N. Y., and Dr. Alice I. Macaulay, Valhalla, N. Y., proposed that therapy with antihypertensive drugs is in its infancy. In from 40 to 50% of carefully selected cases the effects of rapidly progressive hypertension may be reversed by adequate continuous treatment. Careful supervision, a cooperative patient, and a persistent physician are necessary if good results are to be obtained.

"Migraine" is a convenient "wastebasket" nearly full of incorrect diagnoses. Dr. Keith W. Sheldon, Colorado Springs, analyzed a series of 109 patients with a previous definite diagnosis of "migraine" (84 females and 25 males). Careful investigation of this group revealed the following previously unsuspected organic pathology: 9 brain tumors, 18 aneurysms, 2 angiomas, 7 cerebral-vascular disease, 70 cervical-occipital syndromes, 1 subdural hematoma, 1 cervical tumor, and 1 cervical inflammatory tuberculosis. An open mind and patient approach to each headache problem is mandatory.

Dr. Myron Prinzmetal and his associates of Beverly Hills exhibited a variant type of angina pectoris called angina pectoris inversa (API). Classic angina pectoris, as described by Heberden, is a well-defined syndrome with, among others, two

Award Winners

Hektoen Medals.—Hektoen medals, presented to exhibits of original investigation, judged on the basis of originality and excellence of presentation, were awarded as follows:

Gold medal—Alvin L. Watne, Stuart S. Roberts, Ruth G. McGrath, Elizabeth A. McGrew, and Warren H. Cole, University of Illinois College of Medicine, Chicago, for the exhibit illustrating isolation of cancer cells in the circulating blood.

Silver medal—Meyer Texon, New York University Post-Graduate Medical School and Office of the Chief Medical Examiner, City of New York, for the exhibit on the hemodynamic concept of arteriosclerosis.

Bronze medal—Irving S. Cooper, New York University Bellevue Medical Center and St. Barnabas Hospital, New York, for the exhibit on chemopallidectomy for dystonia and other juvenile involuntary movement disorders.

Billings Medals.—Gold, silver, and bronze Billings medals were presented to exhibits judged on the basis of excellence of correlation of facts and presentation rather than upon experimental studies:

Gold medal—C. H. Hodgson, J. A. Callahan, A. J. Bruwer, and A. H. Bulbulian, Mayo Clinic and Mayo Foundation, Rochester, Minn., for the exhibit on misleading thoracic roentgenograms.

Silver medal—Roderick D. Turner, University of California Medical Center, Los Angeles, for the exhibit on surgical technique and uses of isolated intestinal segment in urologic surgery.

Bronze medal—Julio C. Davila, Robert G. Trout, Joseph E. Sunner, and Robert P. Glover, the Thoracic and Cardiovascular Research Laboratory at Presbyterian Hospital, Philadelphia, for the exhibit on cardiac valvular dynamics; anatomic, physiologic and pathologic studies.

Motion Picture Program

The four and one-half day medical motion picture program included 59 general and scientific films, with many of the authors of the films present to introduce and discuss their works.

A unique operation along with an unusual demonstration was filmed by Dr. Max Thorek of Chicago. The patient in the film perforated his esophagus while performing his sword-swallowing act. Closure of the perforation was shown in addition to a professional demonstration of the correct swallowing technique.

The third in a series of six films on medicine and the law was another feature of the film program. Called "The Man Who Didn't Walk," the subject is traumatic neurosis. The film demonstrates the common interest of the medical and legal professions in attempting to evaluate personal injuries resulting from an accident. In another medicolegal film, "Someone Is Watching," attention is called to the various ways in which legal narcotics fall into the hands of dope addicts and peddlers through carelessness and false confidence. The need for diligent safeguarding of drugs was vividly pointed out.

Two of the seven foreign films presented were produced behind the "iron curtain" in Czechoslovakia. One, made under the direction of Dr. Rudolf Malec, illustrates the diagnosis, evaluation, and surgical treatment of intracranial aneurysms. The other described an operative technique on the lung. Both films, made in Prague, were of exceptional quality.

The Technical Exposition

The technical exhibits can best be likened to a "scientific supermarket" where physicians can shop for the latest surgical supplies, office equipment, and medical books as well as accumulate the most recent information on pharmaceuticals. Probably the outstanding attribute of the technical exhibits was the unusual courtesy and patience of the highly trained personnel manning each display.

To help provide a more fundamental understanding of the cell, the basic unit of all life, the Upjohn Company exhibited a plastic model of a human cell magnified more than one million times Physicians were able to walk through the "cell" and observe many phenomena previously described only in textbooks. Eventually the cell will be housed in the Museum of Science and Industry in Chicago.

Wallace Laboratories depicted the path of harmonious life by allowing the physician to walk through a gigantic "breathing chrysalid." Inside the Chrysalida, as it was called by Salvador Dali, its creator, organic forms appear in forced perspective showing the surrealist view of transition from anxiety to tranquility.

A replica of an old time drugstore interior was featured in the Bristol Laboratories exhibit.

Wyeth Laboratories attempted a unique innovation by occasionally converting their technical exhibit into four private conference rooms and inviting visiting physicians to make use of the professional consultative services of the specialists on the Wyeth medical staff.

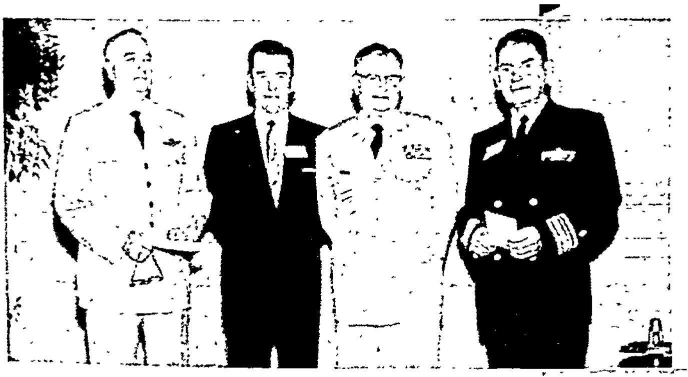
Relaxation was afforded physicians by Pfizer Laboratories. The doctor and his family were given a four-minute chair ride during which time they could observe the development of a pharmaceutical product from research to practice. In the Eli Lilly and Company lounge exhibit, a display of tissue culture methods along with another question and answer display regarding double-blind clinical test procedures, added to the physician's knowledge.

In addition, there were many other exhibitors complementing their presentations of valuable medical information with refreshments and souvenirs that will always be a pleasant reminder to the physician and his family who attended the 1955 A. M. A. annual meeting.

SAN FRANCISCO SCENES—SESSIONS

A view of the throng in the Sheraton-Palace hotel in San Francisco, where Dr. Gunnar Gundersen of LaCrosse, Wis., was inaugurated as the 112th President of the A. M. A.

Dr. E. Vincent Askey of Los Angeles, Speaker of the House of Delegates, joins the immediate Past-President of the A. M. A., Dr. David B. Allman, Mrs. Allman, Rev. Robert D. Vinter, and Dr. Frank Krusen, winner of the A. M. A. 1958 Distinguished Service award.



One of many pre-convention meetings was the Sixth Annual National Medical Civil Defense Conference. These officers took part in discussions: *Left to right,* Air Force Surgeon General Dan C. Ogle; Deputy Surgeon General John D. Porterfield of the Public Health Service; Army Surgeon General Silas B. Hays; and E. C. Kenney, assistant chief of the Navy Bureau of Medicine and Surgery for Professional Operations.

Honored at a luncheon by the Women's Auxiliary and *Today's Health* for exceeding 100% of their quota in the 1957-1958 National T-H Subscription Contest were representatives of the winning state auxiliaries.

SAN FRANCISCO SCENES—EXHIBITS

Above, Dr. Walter G. Spohn of the VA Regional Office in San Francisco discusses his exhibit on plastic artificial eye restoration with Dr. L. V. Johnson of Cleveland.

Left, Dr. Irving S. Cooper's studies of chemopallidectomy for dystonia and related disorders catch the attention of an unidentified youngster with three doctors' wives.

Above, a mass chest survey unit, presented by the Westinghouse Electric Corporation is demonstrated by exhibitor *(right)* to Dr. Robert Warner of Berwyn, Pa., and Dr. Lillian Dunsmore of Downington, Pa.

At a special daily Scientific Exhibit on fresh tissue pathology, Dr. L. R. Grams of San Jose, Calif., points out the features of a diseased kidney to Dr. Elmer Olesky of Los Angeles and Dr. Marvin Brownstein of San Francisco.

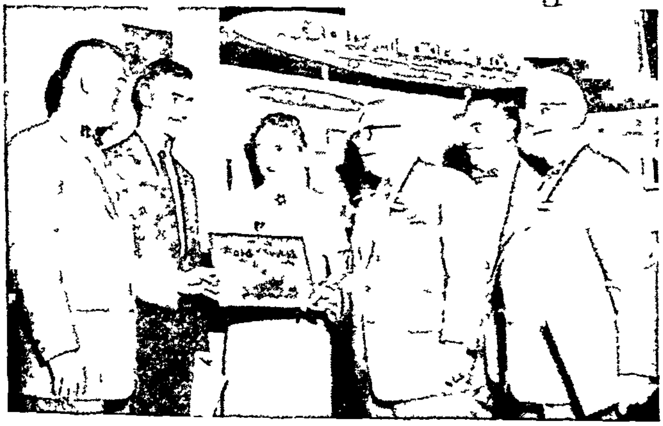
Dr. Dante Bizzari *(standing)* of New York Medical College demonstrates with Joseph Musacchio of Pasadena, Calif., the importance of continuous monitoring of blood pressure, pulse, and heart sounds in a Scientific Exhibit.

SAN FRANCISCO SCENES—HONORS

Right, at the head of the table for a news conference sit Clare L. Chatland of Missoula, Mont., and David R. Brown of Minneapolis, winners of the A. M. A.'s top awards last month in Flint, Mich., at the National Science Fair for scientifically talented high school students.

Left, winners of the Billings gold medal *(left to right),* Drs. A. H. Bulbulian, J. A. Callahan, and A. J. Bruwer of the Mayo Clinic and Mayo Foundation pose with Dr. Alphonse McMahon, Chairman of the Council on Scientific Assembly; Dr. C. H. Hodgson (also a member of the award-winning group); and Dr. Frank B. Queen, Chairman of the Committee on Awards.

Right, winners of the A. M. A. lay Citations for Distinguished Service. Mrs. Charles W. Sewell of Otterbein, Ind., honored for her pioneering work in rural medicine, and Gobind Behari Lal, Ph.D., science editor emeritus for the Hearst newspapers.



Left, winners of the Hektoen gold medal pose before their exhibit. *(Left to right)* Drs. Alvin L. Watne, Stuart S. Roberts, and Elizabeth A. McGrew. With them are Drs. McMahon, Queen, and Thomas G. Hull, Secretary of the A. M. A. Council on Scientific Assembly.

FEDERAL MEDICAL LEGISLATION

2nd Session, 85th Congress

Social Security

S. 3508 by Senator Morse (D., Ore.) is similar to the Forand Bill, H. R. 9467, having the identical provisions for hospitalization, nursing home care, and surgical benefits. It would also periodically increase the tax rate on which social security taxes are paid so that by 1975 the employee and employer each would be paying 5.5% on a wage base of $6,000; this would amount to $330 each. The self-employed would be paying 8.25%, or $495 annually. The bill would also increase the primary and family benefits, based on a new table, to a maximum individual primary benefit of $173.20 and maximum family benefit to $346.40. In addition, there would be an increase in the public assistance, of 25% in the state allotments, for old age assistance, aid to dependent children, aid to the blind, and aid to the permanently and totally disabled. Funds for this increase would come from increased appropriations from general revenues. S. 3646 by Senator Humphrey (D., Minn.) is identical to H. R. 9467, the Forand Bill, and H. R. 10532 by Congressman Dellay (D., N. J.), which has previously been discussed. H. R. 11444 by Congressman Moulder (D., Mo.) and H. R. 11772 by Congressman Blatnik (D., Minn.) are identical to H. R. 9467, the Forand Bill, as are H. R. 10532, 10664, and 11331.

Health, Education, and Welfare

S. 3504 by Senator Neuberger (D., Ore.) would increase the annual authorization for appropriations for Maternal and Child Health Program from 16.5 to 25 million dollars, and for hospital and medical care for the Crippled Children Program from 15 to 25 million dollars.

H. R. 6981 by Congressman Elliott (D., Ala.) and H. R. 6982 by Congressman Fogarty (D., R. I.) are similar to H. R. 10608 by Congressman Fogarty, reported in The Journal, June 7, 1958, page 747; they deal with rehabilitation services for independently living handicapped individuals and assistance in the establishment of public and private nonprofit workshops and rehabilitation facilities. It differs from H. R. 10608 in that funds requested are more modest. A further difference is that H. R. 10608 would provide rehabilitation evaluation service for which the federal government would contribute two-thirds of the cost.

H. R. 11703 by Congressman McCormack (D., Mass.) would amend the public assistance provision of the Social Security Act relating to the provisions of medical care for recipient. This bill would limit the effect of the 1956 amendments and Public Law 85-110 to one fiscal year, terminating on June 30, 1958. Under H. R. 7238, introduced last year by Congressman McCormack, the states could have continued their old programs of direct payments for medical care to the recipient or their pooled fund for vendor payments program and in addition would have provided the $3 per adult and $1.50 per child recipient to be used exclusively for payment to the vendors of medical service. The Senate amended the bill to provide that the states could elect to operate the old vendor plan with federal participation up to the stated maximum or the new $6 and $3 vendor program, but not both. H. R. 11703, in addition, would allow the states to operate their medical care programs as was originally introduced in H. R. 7238, *prior to that bill* being amended by the Senate.

H. R. 11659 by Congressman Dellay (D., N. J.) is identical to H. R. 383 and H. R. 11057 by Congressman Zablocki (D., Wis.) which would establish a Bureau of Older Persons within the Department of Health, Education, and Welfare and would authorize a federal grant to assist in the development and operation of studies and projects to help older persons.

H. R. 11678 by Congressman O'Neill (D., Mass) would amend the public assistance provisions of the Social Security Act to add a fifth category of recipients. The bill would offer grants to states to provide aid to needy persons not eligible for assistance under the present four programs of aid. To qualify for grants, the states would have to operate a state-wide plan, administered by a single state agency that provided for, among other things, financial participation by the state and nondisclosure of beneficiary lists. A state could not qualify for grants if it established as a condition of eligibility (1) an age requirement, (2) a residence requirement, and (3) a citizenship requirement. The federal contribution would equal "one-half of the sums expended . . . as general assistance" and one-half the cost of administering the program. General assistance is defined as "money payments to . . . or medical care . . . or any type of remedial care . . . *in behalf of* needy individuals or families. . . ."

H. R. 11826 by Congressman Coffin (D., Maine) would amend the Hill-Burton Act by providing that a "nonprofit corporation or association which has a formal affiliation with a nonprofit teaching hospital" would be eligible for grants for the construction of diagnostic or treatment centers, provided the grant would be limited to not more than 25,000 per project. Further, these grants would be limited to towns with less than 10,000 population or to groups of towns with an aggregate population of less than 15,000. A "nonprofit teaching hospital" is defined as a hospital properly accredited for internship or residency training, or both.

H. R. 11832 by Congressman McCarthy (D., Minn.) would amend the public assistance provisions of the Social Security Act by doubling the

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From the Washington Office of the American Medical Association.

federal contribution in the medical care vendor payments program from the current $3 per adult and $1.50 per child recipient ($6 to $3 ratio) per month to $6 per adult and $3 per child recipient ($12 to $6 ratio) per month.

H. R. 11835 by Congressman Rodino (D., N. J.) is identical to S. 2994 by Senator Neuberger (D., Ore.), S. 3089 by Senator McNamara (D., Mich.), and H. R. 9822 by Congressman Fogarty (D., R. I.) and provides for a White House Conference on Aging which the A. M. A. supports.

S. 3551 by Senator Hill (D., Ala.) is identical to H. R. 10608 by Congressman Fogarty (D., R. I.) and would broaden the Rehabilitation Act of 1958. (This bill is discussed in THE JOURNAL, 167:747 [June 7] 1958.)

H. R. 11913 by Congressman Roberts (D., Ala.) is similar to H. R. 6874 by Congressman Harris (D., Ark.) and H. R. 7841 by Congressman Fogarty (D., R. I.) and would amend the Public Health Service Act by extending the grant program for research facilities construction by providing grants for the construction, expansion, remodeling, and alteration of teaching and research facilities at new medical and dental schools. The bill would extend for three years the existing law which authorizes 30 million dollars yearly for the construction of research facilities. It would also provide 50 million dollars annually for the next five years to medical, dental, and public health schools for construction of teaching and research facilities. Grants would be up to 50% of cost of construction except where the medical school gives assurances that it would increase the freshman enrollment by 5% during the first year of the program. In such case, the grant could be up to 66⅔% of cost of construction. The bill also provides for a 10-year, 100 million dollar program for grants for the construction of teaching and research facilities at new medical, dental, and public health schools. This would only apply to new schools. Grants up to 66⅔% of cost of construction could be made.

The National Advisory Council would be increased from its present 12 members to 16 members. Six members would be from the public health and 10 from medical, dental, and other health fields. This council would recommend approval of these construction grants to the surgeon general who would have the final approval. The bill further provides that neither the federal government nor any of its officials could interfere with the administration of grantees' institution, personnel, curriculum, methods of instruction, or research. The A. M. A. testified in support of this program with suggested modifications.

S. 3685 by Senator Yarborough (D., Texas) would increase the federal participation in the four public assistance programs. In the aid to the aged, blind, and permanently and totally disabled, the maximum in which the federal government would participate would be increased from the present $60 to $65. The federal government would pay six-sevenths of the first $35 and one-half of the remainder up to $65. In addition, the federal government would pay two-thirds of $8 to provide "medical or any other type of remedial care" for adults receiving benefits under the four aid programs. In the dependent children program, maximum federal participation would be increased to $36 with the federal government paying six-sevenths of the first $21 and one-half of the remainder up to $36. To these funds, the federal government would pay two-thirds of $4 to provide "medical or any other type of remedial care" for children. In addition to these funds, the federal government would pay one-half of the states' administrative costs in carrying out the four programs.

S. 3690 by Senator Anderson (D., N. Mex.) and Langer (R., N. D.) would amend the Public Health Service Act by providing that the surgeon general would make grants to state or local agencies and to universities, hospitals, and laboratories for carrying out projects related to the detection and control of diabetes and for rehabilitating persons suffering from diabetes. It would also provide grants for training and instruction in the treatment of diabetes.

S. 3699 by Senator Langer (R., N. D.) would amend the Hospital Survey and Construction Act in order to make nonprofit corporations or associations having a contractual affiliation with a nonprofit hospital approved for internship or residency training eligible for construction grants under the Hill-Burton amendment.

Antirecession

H. R. 11445 by Congressman Rivers (D., S. C.) is identical to H. R. 10610 by Congressman Gregory (D., Ky.) and H. R. 10706 by Congressman Roberts (D., Ala.), reported in the June 7, 1958, issue of THE JOURNAL, page 747; it would extend the time for hospital construction loans under the Housing Act of 1956 for construction of community facilities (including hospitals) in areas designated by the Office of Defense Mobilization.

H. R. 11474 by Congressman Spence (D., Ky.) is similar to S. 3497 by Senator Fulbright (D., Ark.) and H. R. 11272 by Congressman Rains (D., Ala.) and would establish an emergency community facilities and public works program in the Community Facilities Administration of the House and Home Finance Agency.

H. R. 11774 by Congressman Blatnik (D., Minn.), H. R. 11465 by Congressman Porter (D., Ore.), and H. R. 11737 by Congressman Dent (D., Pa.) are identical to H. R. 10570 by Congressman McCarthy (D., Minn.) on Revision of Unemployment Compensation Plans previously discussed. (See THE JOURNAL, June 7, 1958 issue, pp. 747-750, for reference to bills previously discussed.)

H. R. 11902 by Congressman Blatnik (D., Minn.) is virtually identical to H. R. 11474 by Congressman Spence (D., Ky.) and S. 3497 by Senator Fulbright (D., Ark.), except for two provisions. This bill provides that "all functions, powers, duties . . . with respect to health, refuse disposal, sewage treatment and water purification shall be exercised by . . . the Surgeon General of the Public Health Service." The bill also provides that the provision of the Davis-Bacon Act relating to local wage rates shall be in effect on projects constructed under this loan program.

Veterans' Affairs

H. R. 11660 by Congressman Kearney (R., N. Y.) would authorize outpatient care for non-service-connected disabilities to veterans with a service-connected disability rating of 30% or more and to veterans who are in receipt of a pension for a non-service-connected disability.

H. R. 11837 by Congressman Saylor (D., Pa.) is identical to H. R. 6716 by Congressman Kee (D., W. Va.) and H. R. 10748 by Congressman Beckworth (D., Texas), previously discussed, and which would prohibit the termination of any 10% or more, and 10 years or more, service-connected disability rating for compensation, pension, and insurance purposes.

S. 3599 by Senator Langer (R., N. D.) would extend the presumption of a service-connection for multiple sclerosis from the present two years after discharge to seven years.

H. R. 12001 by Congressman Siler (R., Ky.) would provide for emergency outpatient treatment for any disability, whether service-connected or not, to a veteran who is receiving a pension or compensation. The bill also provides that the VA would reimburse any such veteran for the expense incurred in acquiring emergency outpatient treatment at any hospital certified by the American Hospital Association.

Tax Relief

S. 3527 by Senator Hill (D., Ala.) is similar to [illegible]32 and others providing for tax exemption for [illegible]er education of $600 annually for the taxpayer, [illegible] spouse, or for dependents provided they attend an institution of higher education during at least four calendar months and provided the institution has met certain requirements.

H. R. 11788 by Congressman Quie (R., Minn.) is identical to S. 3194 by Senator Sparkman (D., Ala.) (J. A. M. A. *166*:2188 [April 26] 1958) and similar to H. R. 10499, 11617, and 10781 providing tax deferment for annuities.

H. R. 11812 by Congressman Flood (D., Pa.) providing a tax credit for higher education is similar to H. R. 11393 by Congressman Cramer (R., Fla.), previously discussed, and H. R. 490 and 765.

Union

S. 3618 by Senator McClellan (D., Ark.), known as the Labor Union Registration Act of 1958, would require the registration of labor unions and labor relations counselors. It provides minimum requirements for bylaws for unions required to file under the bill. It sets forth what information would have to be filed with the Secretary of Labor by unions and provides for keeping the registration statement current. Penalties are provided for violations. One requirement would be the registration of the name and title of each trustee or person responsible for the administration of any trust in which a labor union is interested. A "trust in which a labor union is interested" would include welfare and pension plans.

Miscellaneous

S. 3544 by Senators Mansfield (D., Mont.) and Bridges (R., N. H.) on Reorganization of the Defense Department is identical with H. R. 11001, 11002, and 11003 previously reported. H. R. 11472 would amend the Water Pollution Control Act. It is similar to S. 3481 by Senator Purtell (R., Conn) also previously reported and differs in that it would increase the amount of federal participation on projects, would increase the grants from 30% of the cost or $250,000 to 50% of the cost, or $500,000, whichever is smaller, and if the project were being carried out by two or more cities or political subdivisions, the federal participation could be multiplied by the number of entities involved. It would also increase the annual authorization to carry out the provisions of the act from 50 to 150 million dollars and increase the statutory limitation which determines the life of the act from 500 million to 1.5 billion dollars.

H. R. 11714 by Congressman Blatnik (D., Minn.) is identical to the bills mentioned regarding the Water Pollution Control Act, with the exception that annual authorizations are only increased from 50 to 100 million dollars, and the statutory limitation from 500 million to one billion dollars.

S. 3649, the Administration Bill, by Senator Saltonstall (R., Mass.) and H. R. 11958 by Congressman Martin (R., Mass.) would provide for the Defense Department Reorganization. Among other things, it would reduce the number of Assistant Secretaries of Defense from nine to seven and would repeal Reorganization Plan no. 6 of 1953 under which the Office of the Assistant Secretary of Defense (Health and Medical) was established. While the bill does not specify which Assistant Secretary of Defense would be eliminated, indications are that the Office of the Assistant Secretary of Defense (Health and Medical) would be abolished and the position relegated to that of a special assistant to the Secretary of Defense.

H. R. 11960 by Congressman Knutson (D., Minn.) is the Omnibus Education Act of 1958.

A. M. A. ADOPTS NEW CODE FOR DOCTORS AND LAWYERS

A new "National Interprofessional Code for Physicians and Attorneys" was approved by the A.M.A. House of Delegates at its Annual Meeting in San Francisco. The code will serve as a suggested guide for physicians and attorneys in their inter-related practice in the areas covered by its provisions—subject to the principles of medical and legal ethics and the rules of law prescribed for their individual conduct.

The code was formulated by a joint national medicolegal liaison committee made up of representatives appointed by the American Bar Association and the American Medical Association. The three medical representatives include Drs. David B. Allman, Hugh Hussey, and George Fister. In addition to drawing up this new code, the joint committee has considered such things as the encouragement of state and local medicolegal meetings, medical professional liability problems, medicolegal forms, and the possibility of establishing medicolegal courses in law schools and medical schools. The same code will be presented for approval to the Board of Governors and the House of Delegates of the American Bar Association at its meeting in August.

In the preamble the code states that it "will serve its purpose if it promotes the public welfare, improves the practical working relationships of the two professions, and facilitates the administration of justice." Various sections cover such topics as medical reports; conferences between the physician and the attorney; subpoena for medical witness; arrangements for court appearances; physician called as witness; fees for services of physician relative to litigation; payment of medical fees; implementation of the code at state and local levels; and consideration and disposition of complaints.

COUNCIL ON MEDICAL SERVICE

STUDY OF PERINATAL MORTALITY AND MORBIDITY PROGRAMS IN THE UNITED STATES

PART 3

HENNEPIN COUNTY (MINNESOTA) PERINATAL MORTALITY STUDY

Beginning in 1950 certain information relating to prematurity, congenital malformation, birth weight, and weeks of gestation was included on the revised birth and stillbirth certificates. From this information the Minnesota Department of Health was able to compile data which indicated, to some degree, the problems which could be emphasized in a study designed to promote further reduction of infant mortality. It was shown that 76% of infant deaths occurred less than one month after birth and that 70% were due to or associated with prematurity, congenital malformation, or birth injury. These facts, together with the effectiveness and acceptance of the maternal mortality study in Minnesota, prompted the state department of health to propose a pilot study on neonatal mortality in Hennepin County, which includes Minneapolis. This proposal was in turn submitted to, and approved by, the Child Health Committee of the Minnesota State Medical Association, the council of this association, and the Hennepin County Medical Society. The Northwest Pediatric Society appointed three members to the proposed committee, as did the Hennepin County Medical Society. Along with representatives from the maternal and child health section of the Minnesota Department of Health, these constituted the nucleus of the study committee.

Other interested groups were contacted and agreed to help sponsor the proposed study. The Hennepin County neonatal mortality study began on Jan. 1, 1952, as a cooperative undertaking of the Hennepin County Medical Society, the Minneapolis Pediatric Society, the Minneapolis Obstetric Society, the Minneapolis chapter of the American Academy of General Practice, the Minneapolis Health Department, the Minneapolis Hospital Council, the departments of pediatrics and pathology of the University of Minnesota Medical School,

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This is the third of a series of articles prepared by the Committee on Maternal and Child Care of the Council on Medical Service on perinatal mortality and morbidity study programs that are being conducted in various parts of the United States. Subsequent articles will appear in THE JOURNAL from time to time.

Committee members are W. L. Crawford, M.D., Chairman, Rockford, Ill.; R. B. Chrisman Jr., M.D., Coral Gables, Fla.; Philip S. Barba, M.D., Philadelphia; Harold S. Morgan, M.D., Lincoln, Neb.; Garland D. Murphy, M.D., El Dorado, Ark.; Howard A. Nelson, M.D., Greenwood, Miss.; J. L. Reichert, M.D., Chicago; Donald A. Dukelow, M.D., Consultant, Chicago; Philip F. Williams, M.D., Consultant, Bala Cynwyd, Pa.; Edwin J. Holman, Consultant, Chicago; and Mr. George W. Cooley, Secretary, and Mr. Donald B. Berg, Research Assistant, Chicago.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

THE PRESENT AND FUTURE STATUS OF FOREIGN MEDICAL SCHOOL CREDENTIALS IN THE UNITED STATES

Since February 1950, the Council on Medical Education and Hospitals of the American Medical Association and the Executive Council of the Association of American Medical Colleges have published a list of foreign medical schools whose graduates are recommended for consideration on the same basis as graduates of approved medical schools in the United States and Canada. This has always been offered as an advisory list for the use of State Licensing Boards, Hospitals, Specialty Boards and other organizations in the United States concerned with the evaluation of medical credentials and qualifications of graduates of foreign medical schools. These same organizations have always been advised that the list was acknowledged to be a tentative one and that the position of the Councils with respect to the foreign medical schools not listed has been that they neither approve nor disapprove of them.

In the years since the initial publication of this list, the number of graduates of foreign medical schools coming to the United States on either temporary or permanent visas has increased tremendously. The vast majority of physicians now entering this country either for further study as interns or residents or for permanent stay and medical licensure have received their medical degrees from medical schools other than those listed.

It is impossible for the Council on Medical Education and Hospitals of the American Medical Association and the Executive Council of the Association of American Medical Colleges to obtain and maintain adequate and current information concerning the educational programs of all or even a reasonable portion of the medical schools in the world whose graduates will now and in the future wish to come to the United States. For this reason, the two Councils many months ago reached the decision that it was no longer feasible to maintain a recommendation regarding graduates of foreign medical schools based on the school of graduation. After considerable study, it was concluded that a mechanism for the evaluation of the medical credentials and qualifications and facility with the English language of the individual foreign physician would be more generally equitable to graduates of all foreign medical schools desiring to enter this country. A program of this kind would also better serve the welfare of American patients for whose care these physicians would have responsibility.

The Educational Council for Foreign Medical Graduates

After more than two years of cooperative study by representatives of the American Hospital Association, the American Medical Association, the Association of American Medical Colleges, and the Federation of State Medical Boards of the United States, a method for evaluating the graduates of foreign medical schools wishing to come to the United States has been devised. The four parent groups have sponsored the organization of the Educational Council for Foreign Medical Graduates (ECFMG) to implement this new program. The Educational Council for Foreign Medical Graduates (ECFMG) has been legally incorporated in the State of Illinois and is located at 1710 Orrington Avenue, Evanston, Illinois. Responsibility for the affairs of ECFMG rests with a 10 member Board of Trustees which includes two members each selected by the American Hospital Association, the American Medical Association, the Association of American Medical Colleges, the Federation of State Medical Boards of the United States and two representatives-at-large (one selected by the United States Department of Health, Education and Welfare and one by the United States Department of Defense).

ECFMG will evaluate the medical credentials of graduates of foreign medical schools wishing to enter the United States. Credentials will be declared acceptable if they indicate that the foreign graduate has completed no less than 18 years of formal education including at least 4 academic years in a bona fide medical school. For candidates whose credentials are acceptable, ECFMG will test their knowledge of medicine and command of English through testing centers in the United States and abroad. Those candidates who are successful will be certified as possessing medical knowledge reasonably equivalent to that expected of graduates of approved medical schools in the United States and Canada and as having satisfactory facility with the English language. The certification so acquired will be transmitted to hospitals, licensing authorities, specialty boards and other appropriate organizations or institutions as desired by the candidates.

Authorized by the Council on Medical Education and Hospitals, A. M. A., and the Executive Council, Association of American Medical Colleges.

It is to be emphasized that ECFMG (and also the Council on Medical Education and Hospitals of the American Medical Association and the Executive Council of the Association of American Medical Colleges) is not designed to serve as a placement agency. Graduates of foreign medical schools must continue to make arrangements for placement in U. S. hospitals through direct correspondence with the hospital(s) concerned. Assistance in placement may also be obtained through the National Committee for Resettlement of Foreign Physicians, Inc., 31 Union Square West, New York 3, N. Y.

Further information regarding the program of ECFMG, procedure for making application, dates and locations for testing, fees, etc., can be obtained by corresponding directly with the Educational Council for Foreign Medical Graduates, 1710 Orrington Avenue, Evanston, Illinois.

The Present and Future Status of the List of Foreign Medical Schools

In February 1958, the Council on Medical Education and Hospitals of the American Medical Association and the Executive Council of the Association of American Medical Colleges acted to withdraw the current list of foreign medical schools for whose graduates the Councils have recommended consideration on a basis comparable to that of graduates of approved medical schools in the United States and Canada. *The withdrawal of this list and its accompanying recommendation is to become effective as of January 1, 1960.*

The Councils wish to emphasize that this notice of discontinuing the listing of certain foreign medical schools is not intended to indicate any lowering of standards of the foreign medical schools that have been on the list. Rather, this action reflects the Councils inability to acquire and maintain a continuing, adequate knowledge of the educational programs of all the foreign medical schools whose graduates come to the United States.

The Council on Medical Education and Hospitals of the American Medical Association and the Executive Council of the Association of American Medical Colleges now recommend that licensing boards, hospitals, specialty boards and other organizations in the United States concerned with the medical qualifications of graduates of foreign medical schools, *consider certification by the Educational Council for Foreign Medical Graduates as evidence that the recipient of such certification is possessed of medical knowledge comparable to that expected of graduates of approved medical schools in the United States and Canada.* These two Councils further recommend that *such certification be considered as evidence of the quality of medical training offered by the medical school attended by the holder of a certificate at the time of his graduation.*

In the interval between the present and the January 1, 1960 effective date of withdrawal of the list of foreign medical schools, the Councils will support the recommendation in regard to graduates of the listed schools and also the recommendation pertaining to certification by the Educational Council for Foreign Medical Graduates. The Councils believe that the transition period of almost two years should allow adequate opportunity for all concerned to adapt to this new program.

The Present and Future Status of Graduates of Foreign Medical Schools Seeking Advanced (Internship and Residency) Training in the United States Under the Exchange-Visitor Program

The Council on Medical Education and Hospitals of the American Medical Association will revise in the near future its Essentials of an Approval Internship and Essentials of Approved Residencies and Fellowships to include a statement to the effect that hospitals considering foreign medical school graduates for internship or residency positions are recommended to acquire reasonable assurance regarding the medical qualifications of foreign trained physicians by deferring their appointment until the candidates have been certified by ECFMG.

It is expected that this revision will be effective for intern and residency appointments to begin on and after January 1, 1960. Since graduates of foreign medical schools accepting appointments as interns and/or residents in the interval period before January 1, 1960 are likely to consider seeking reappointment after that, it is suggested that where possible they avail themselves of the opportunity of evaluation by ECFMG before that date. *Regardless of the date of appointment, it is expected that all graduates of foreign medical schools serving as interns or residents in U. S. hospitals as of July 1, 1960 will have been certified by ECFMG.*

The Present and Future Status of Graduates of Foreign Medical Schools Entering the United States on Permanent (Immigration) Visas

Neither the Council on Medical Education and Hospitals of the American Medical Association nor the Executive Council of the Association of American Medical Colleges is in a position to render advice concerning the basic privilege of immigration. Information concerning immigration to the United

States can be obtained from the nearest United States Consulate or Embassy or from the Immigration and Naturalization Service of the United States Department of Justice.

Medical licensure in the United States is a "state right" and is entirely under the jurisdiction of the governments of the individual states. The power to license physicians is exercised through the medical licensing boards of each individual state and there is no licensure of physicians in this country by the federal government. It is not possible for either Council or for ECFMG to intervene on behalf of any individual seeking licensure whose credentials do not meet the requirements of the board to which he has applied. ECFMG will, however, on request of the foreign trained physician notify any board of his certification acquired through the new evaluation program.

The material for a summary of the present requirements of the various states, territories and possessions for medical licensure of foreign medical graduates is collected annually by the Council on Medical Education and Hospitals and published in The Journal of the American Medical Association. Current and more detailed information should be obtained through direct correspondence with the secretaries of the boards in those states in which the foreign medical graduate is most interested.

Graduates of foreign medical schools contemplating immigration to the United States for the practice of medicine should note that one requirement of the vast majority of states is an approved internship in the United States. It is anticipated that hospitals offering approved internships will request that graduates of foreign medical schools seeking such positions on and after January 1, 1960 will have obtained certification by ECFMG. It appears likely that some hospitals may expect such certification prior to that date. *Regardless of the date of appointment, it is expected that all graduates of foreign medical schools serving as interns or residents in U. S. hospitals as of July 1, 1960 will have been certified by ECFMG.*

The Federation of State Medical Boards of the United States helped create and strongly supports the program of the Educational Council for Foreign Medical Graduates and it is anticipated that increasing numbers of individual medical licensing boards will require certification by ECFMG as prerequisite to licensure examination for foreign medical graduates. It is likely that by January 1, 1960 many and perhaps most licensing boards will have established this requirement.

Present and Future Status of American Citizens Studying Medicine Outside the United States and Canada

American citizens undertaking their medical studies abroad have been subject to the same regulations and procedures governing medical licensure and intern and residency positions as are all other graduates of foreign medical schools. Therefore, Americans enrolled in medical schools outside the United States and Canada who plan to return to this country for internship, residency and/or medical licensure are encouraged to seek certification by ECFMG on completion of medical school studies. Comments appearing above concerning the relationship between ECFMG and internship and residency positions and medical licensure for foreign medical graduates entering the United States on permanent visas are equally applicable to American citizens studying medicine abroad.

Policy of the American Hospital Association *Concerning Graduates of Foreign Medical Schools*

The American Hospital Association has strongly supported the organization and efforts of the Educational Council for Foreign Medical Graduates. It believes that only qualified medical graduates should serve in patient care situations in hospitals. To this end, it now advises hospitals considering appointment of foreign medical graduates to their staffs, wherever they can do so with fairness to themselves and to the foreign medical graduate, to accept only foreign medical graduates certified by the Educational Council for Foreign Medical Graduates.

It is expected that all graduates of foreign medical schools serving as interns or residents in U. S. hospitals as of July 1, 1960 will have been certified by ECFMG. The American Hospital Association will take this into consideration when approving hospitals for listing.

Policy of the National Intern Matching Program Concerning Graduates of Foreign Medical Schools

The vast majority of graduates of American medical schools acquire internship appointments through a matching program which assures them a position in the first hospital of their choice that ranks the graduate high on its list of prospective interns. In the past, the National Intern Matching Program, 2530 Ridge Avenue, Evanston, Illinois, has accepted graduates of foreign medical schools. It will continue to do so beginning with the 1959-1960 program, provided the foreign medical graduate has been certified by the Educational Council for Foreign Medical Graduates. Information regarding the National Intern Matching Program can be obtained at the address given above.

MEDICAL NEWS

CALIFORNIA

Library on Air Pollution Control.—The six-county Bay Area Air Pollution Control District, San Francisco, has opened a technical library of nearly 7,000 microfilmed articles, available with a microfilm reader, for the free use of the public in the Bay Area, for answers to problems on the measurement, effects, and control of air pollution. The library was compiled by Stanford Research Institute under the supervision of control officer Benjamin Linsky and technical literature specialist Gloria Smith. The material may not be checked out, but a photocopy machine is set for use in conjunction with the microfilm reader so that copies of pages can be made.

DELAWARE

Community Honors Dr. Chipman.—About 450 citizens of Harrington honored Dr. William T. Chipman on Feb. 24 after 45 years of the practice of medicine. The introduction presented by the mayor of Harrington, Dr. Hewitt W. Smith, past-president of the Medical Society of Delaware, read in part: "Dr. Chipman has seen fit to discharge his civic responsibilities to the community as manifest by his past activities in: the Harrington Building and Loan Association, Vice-Presidency of The First National Bank, first President of the Harrington Chamber of Commerce, Director of The Kent and Sussex Fair Association, Speaker of the House of Representatives."

FLORIDA

Society News.—The Greater Miami Eye, Ear, Nose and Throat Society has elected the following officers for 1958: president, Dr. William Steinman; president-elect, Dr. James H. Mendel Jr.; and secretary-treasurer, Dr. Herbert C. Howard. The society meets quarterly at the Urmey Hotel in Miami.——The Florida Radiological Society has installed the following officers for the year 1958-1959: president, Dr. Charles R. DeArmas, Daytona Beach; vice-president, Dr. John P. Ferrell, St. Petersburg; secretary-treasurer, Dr. Russell D. D. Hoover, West Palm Beach; councilor to American College of Radiology, Dr. James M. Dell Jr., Gainesville; and alternate councilor, Dr. Oliver P. Winslow Jr., Miami.——The officers of the Greater Miami Radiological Society are: president, Dr. Alfred G. Levin; vice-president, Dr. Andre S. Capi; and secretary-treasurer, Dr. George P. Daurelle Jr. Society meetings are held on the third Wednesday of each month at 8 p. m. at Jackson Memorial Hospital.

ILLINOIS

Tuberculosis in Suburban Cook County.—The Suburban Cook County Tuberculosis Sanitarium District has reported that during 1957, a 10% increase over the previous year developed in the total number of new active cases of tuberculosis reported in the area. During 1957 there was also an 11.1% increase in the total number of persons hospitalized with active tuberculosis in the facilities provided through the sanitarium district. The increase in the incidence of tuberculosis became evident during the last few months of 1957. The total number of persons hospitalized by the suburban tuberculosis district is higher than at any time during the last five-year period. Physicians may refer their patients to any of the six chest clinics of the district throughout suburban Cook County. Inquiries may be made through Dr. Edward A. Piszczek, Field Director, the Suburban Cook County Tuberculosis Sanitarium District, 7556 W. Jackson Blvd., Forest Park. Telephone: FOrest 6-5000.

Chicago

Dr. Atwood to Head Genetics Program.—Dr. Kimball Chase Atwood, of the Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tenn., has been named to head the work in medical genetics at the University of Chicago. Dr. Atwood was research associate in zoology at Columbia University from 1947 to 1950. He has been senior biologist at the Oak Ridge National Laboratory since 1951.

I. F. Volini Memorial Lectureship Fund.—Dr. John F. Sheehan, dean, Stritch School of Medicine of Loyola University, announces the establishment of a memorial lectureship fund in honor of Dr. Italo Volini, who was a member of the faculty for 30 years and chairman of the department of medicine for 20 years preceding his death in 1950. Friends interested in supporting this lectureship are requested to send their contributions to the Office of the Dean, Stritch School of Medicine, 706 S. Wolcott, Chicago 12.

Home for Foundlings and Unwed Mothers.—The Chicago Foundlings Home presents to the unwed mother a protective, rounded maternity home service; temporary nursery care for the infants surrendered to the agency; and an adoption program for the mothers who wish to use it. Homemaking is

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

offered in lieu of a fee. It was founded in 1871 as a hospital for abandoned babies and mothers by the late Dr. George E. Shipman. On recommendation of a physician, the home will accept expectant mothers at any stage of their pregnancy. Medical care can be arranged with neighboring clinics in accordance with the mother's desire. A new home currently is being planned in the medical center which will be located at 1720 W. Polk St. Dr. Karl A. Meyer is president of the board of trustees.

Researchers Awarded Honorary Degrees.—Three medical researchers have been awarded honorary doctor of science degrees by the University of Chicago: George W. Corner, member of the Rockefeller Institute for Medical Research, New York City; Nicholson J. Eastman, chairman, department of obstetrics and gynecology, Johns Hopkins Medical School, Baltimore; and Richard E. Shope, member of the Rockefeller Institute for Medical Research. Chancellor Lawrence A. Kimpton conferred the degrees. Dr. Corner has done research in embryology which led to detailed studies in the physiology of reproduction and his isolation and purification of progesterone, done in collaboration with Dr. Willard M. Allen. Dr. Eastman, who has concentrated his work on the human fetus and the toxemias of pregnancy has been chairman of the committee on maternal and child health services of the Children's Bureau and of the Committee on Maternity Care of the World Health Organization. Dr. Shope has among his discoveries the virus of swine influenza and its complicated route of transmission, and two rabbit tumors produced by viruses.

INDIANA

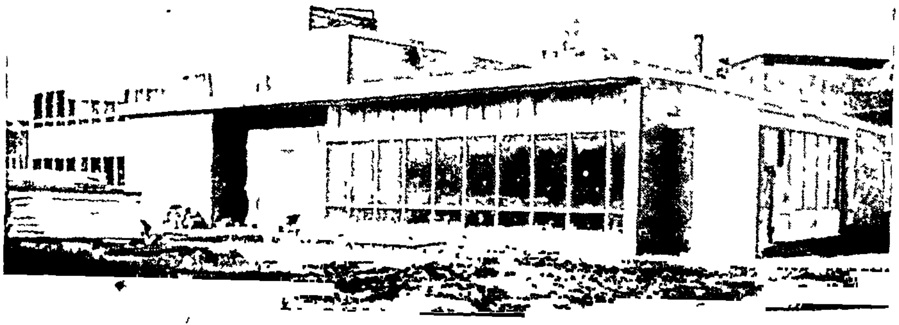
Society News.—Dr. Stephen L. Johnson, Evansville, was named the first president of the permanent organization of the Indiana Society of Internal Medicine at an organizational meeting March 9. Dr. Sherman L. Egan, South Bend, was elected president-elect for 1959; Dr. William D. Province, Franklin, vice-president; Dr. E. Paul Tischer, Indianapolis, secretary-treasurer; and Drs. Arthur B. Richter, Indianapolis, John F. Ling, Richmond, Robert B. Sanderson, South Bend, and George W. Willison, Evansville, councilors.——The officers of the Indiana Roentgen Society for the coming year are: president, Dr. Wallace D. Buchanan, South Bend; president-elect, Dr. John R. Lionberger Jr., South Bend; secretary-treasurer, Dr. Chester A. Stayton Jr., Indianapolis. Meetings are held twice a year, the first Sunday in May and during the fall meeting of the Indiana State Medical Association.

KANSAS

Personal.—Dr. Lewis L. Robbins, chairman, psychotherapy research project, Menninger Foundation, Topeka, and secretary, American Psychoanalytic Association, has been appointed director of professional services of Hillside Hospital, Glen Oaks, N. Y., effective July 1, 1958.

MICHIGAN

New Headquarters for Wayne County Society.—On May 28 the Wayne County Medical Society moved to its new headquarters, the new David Whitney House, a two-story, air-conditioned, gray-brick building, located in an area which includes the Lafayette Clinic–Receiving Hospital, Memorial Hospital, the Kresge Eye Institute, and a planned medical library. The cost of the building, about $830,000, have been paid, but a 10-year loan has been arranged to pay for the furnishings, equipment, and parking area, costing about $150,000. The ground floor has an auditorium with a seating capacity of 417. The first floor has a dining room that can seat 300, and the executive offices are located on the second floor. Plans for the new headquarters started in 1947 with the appointment of a building committee. In 1953 Gordon H. Scott, Ph.D., dean, Wayne State University Medical School, offered the society a free building site on the grounds of the school, and it was accepted. The ground-breaking ceremony was held Dec. 19, 1956, and the cornerstone was laid Oct. 4, 1957. The donors of the original headquarters, David Whitney House, specified that in case of sale the proceeds should be used for a new building to be known by the same name.


New Headquarters of the Wayne County Medical Society, Detroit.

Society News.—Officers of the Michigan Allergy Society elected for the coming year are Dr. Bernard Dickstein, Flint, president; Dr. Milton J. Steinhardt, Detroit, vice-president; and Dr. Robert G Lovell, Ann Arbor, secretary-treasurer.——The Detroit Dermatological Society has elected the following to office for the year 1958-1959: president, Dr. George B. Sexton, London, Ontario; president-elect, Dr. Alice E. Palmer; secretary-treasurer, Dr. Alice E. Palmer; and recorder, Dr. Robert E. Burns.—The 1958-1959 officers of the Michigan Society of Neurology and Psychiatry and the Michigan District Branch of the American Psychiatric Association are as follows: president, Dr. Benjamin Barenholtz, Detroit; president-elect, Dr. Ivan A. LaCore, Pontiac; secretary, Dr. Eugene J. Alexander, Detroit; and treasurer, Dr. John A. Belisle, Eloise.

MINNESOTA

Honor Eleven Emeritus Staff Members.—At ceremonies May 23 at the University of Minnesota, Minneapolis, president James Morrill paid tribute to the following men who, in recent months, have reached emeritus status on the staff of the Mayo Clinic and the faculty of the University: Dr. Virgil S. Counseller, Dr. Claude F. Dixon, Hiram E. Essex, Ph.D., William H. Feldman, M.S., Dr. Frederick A. Figi, Dr. Ralph K. Ghormley, Dr. Samuel F. Haines, Dr. Philip S. Hench, Dr. Richard M. Hewitt, Dr. Bayard T. Horton, and Dr. James F. Weir. The 11, who hold academic rank of professor or associate professor, represent a total of several hundred years to the university. Text of the certificate for meriti reads in part: "The Regents and the President of the University of Minnesota, in recognition of devoted service, express their gratitude and high esteem through the presentation of this Certificate of Merit. . . ."

Dr. Robert Howard Succeeds Dr. Diehl as Dean.—Promotion of Dr. Robert B. Howard to be dean of the University of Minnesota's college of medical sciences succeeding Dr. Harold S. Diehl, who retired June 30, has been announced. Dr. Howard has been associate dean since last fall when Dr. Diehl took leave of absence to accept appointment with the American Cancer society as senior vice-president for research and medical affairs and deputy executive vice-president. Dr. Diehl had been dean since 1935. Dr. Howard was a teaching fellow in medicine at the university in 1945; in 1948 he became an instructor in medicine, then was promoted to assistant professor, associate professor, and professor, the last promotion having been July 1. Continuing as assistant deans are Drs. N. L. Gault Jr., and Henry M. Cavert. Dr. Gault succeeded Dr. Howard last fall as director of continuation medical education and will serve as a full-time assistant dean.

NEW HAMPSHIRE

Society News.—The New Hampshire Society of Anesthesiologists recently elected the following officers: president, Dr. John F. Archibald, Plymouth; vice-president, Dr. Robert W. Ballantyne, Windsor, Vt.; and secretary-treasurer, Dr. Agnes V. Bartlett, Springfield, Vt.

at least three weeks [illegible]

NEW MEXICO

State Medical Election.—The New Mexico Medical Society has elected the following new officers: president, Dr. James C. Sedgwick, Las Cruces; president-elect, Dr. Lewis M. Overton, Albuquerque; vice-president, Dr. Allan L. Haynes, Clovis; councilor for District III, Dr. Guy Rader, Albuquerque; councilor, District VI, Dr. William J. Hossley Jr., Deming; delegate to A. M. A., Dr. Earl L. Malone, Roswell; and alternate delegate, Dr. Samuel R. Ziegler, Espanola.

Personal.—Dr. Henry C. Jernigan, director at large, National Tuberculosis Association Board of Directors, has been appointed medical director of the Fort Staunton Tuberculosis Hospital, Fort Staunton.

NEW YORK

Grant for Radiation Therapy Center.—A John A. Hartford Foundation grant of $203,200 toward a $400,000 Radiation Therapy Center which the University of Rochester will build for the Strong Memorial Hospital at the university's Medical Center has been announced. Completion of the project is expected early next year. The Hartford Foundation grant provides for purchase of equipment and payment of part of the estimated $150,000 annual operating costs of the center for three years. The university will provide a new building and pay the balance of the operating expenses. Director of the radiation center will be Dr. Philip Rubin, chief, division of radiation therapy. The Hartford Foundation, with offices in New York City, was founded by the late Mr. John A. Hartford, who was president of the Great Atlantic & Pacific Tea Company for many years.

Society News.—The Radiological Society of the State of New York has elected the following officers: Dr. John F. Roach, of Loudonville, president and chairman of the section on radiology; Dr. Frederick H. Lutze, New Rochelle, vice-president; and Dr. Mario C. Gian, Buffalo, secretary-treasurer.—At the annual meeting of the New York Academy of Gastroenterology the following officers were elected for 1958-1959: president, Dr. Milton J. Matzner, Brooklyn; president-elect, Dr. Michael Weingarten, New York City; first vice-president, Dr. Joseph R. Van Dyne, Forest Hills; second vice-president, Dr. Hyman M. Robinson, Brooklyn; secretary, Dr. Alexander Slanger, Brooklyn; recording secretary, Dr. Jerome Weiss, New York City; treasurer, Dr. William C. Jacobson, New York City; and chairman, Board of Trustees, Dr. Harry Barowsky, New York City.—The New York Tuberculosis and Health Association, Inc., has moved its offices to 260 Fourth Ave., New York 10. The new telephone is ORegon 3-3935.

Personal.—Dr. Edward C. Reifenstein Sr., former chairman, department of medicine, State University College of Medicine in Syracuse, was honored by physicians who trained under him at a testimonial dinner May 8.——Dr. Leonard D. Fenninger, assistant dean, University of Rochester School of Medicine and Dentistry has been promoted to associate dean and associate professor of medicine and senior associate physician in Strong Memorial Hospital, effective July 1.——Jack M. Wolfe, Ph.D., chairman, department of anatomy, Albany Medical College, received an honorary doctor of science degree from his alma mater, Carson-Newman College, in Jefferson City, Tenn., May 30.

New York City

Gift for University Hospital.—The James Foundation of New York has made a gift of $110,000 to New York University-Bellevue Medical Center toward the construction of a 10-story, 600-bed University Hospital, on the center's campus. Contributions totaling $250,000 have been made by the James Foundation to the medical center since it began its development program in 1948. The current gift will release a similar amount of money from the Samuel H. Kress Foundation which has pledged 5 million dollars on a dollar-for-dollar matching plan toward the construction of the new hospital.

Personal.—Dr. Raymond S. Jackson, associate professor of medicine, New York University Post-Graduate Medical School, has been appointed administrator of university hospital of NYU-Bellevue Medical Center, succeeding Mr. Franklin P. Iams, who will become administrator of the proposed Fairfax County Hospital in Virginia. Dr. Jackson is currently special assistant to the director of the medical center and coordinator of planning for a new 600-bed, 19-story University Hospital which he will administer when completed.——Dr. Theodore R. Miller spoke before the staff of the Ziv Hadassah Hospital in Jerusalem on May 19 on hepatic lobectomy.——Dr. Harry Bakwin, professor of clinical pediatrics, New York University-Bellevue Medical Center, delivered the annual Otto A. Faust Lecture at Albany Medical College, May 15 on "Research Approaches to Child Psychiatry." The lecture honors Dr. Otto A. Faust, who is professor of pediatrics and a former chairman of the department at Albany Medical College.——Dr. Alexander W. Kruger, former manager, Brooklyn Veterans Administration Hospital, has been appointed Health Services Consultant of the National Committee on the Aging, a standing committee of the National Social Welfare Assembly. Recently, the committee received $500,000 from the Ford Foundation to expand its work.

NORTH CAROLINA

Program at Duke to Train Medical Researchers.—Plans for a major educational program designed to produce physicians who are also skilled medical research scientists have been announced at Duke University by Dr. Wilburt C. Davison, dean of the School of Medicine. The program is planned primarily to train medical students and hospital resident physicians in methods and use of research tools for scientific investigation. Financial support during the first three years of operation will come from combined grants totaling more than three-quarters of a million dollars. About $500,000 will be used to provide quarters and equipment for the program, while the remainder will cover salaries and operating expenses. The objective is to intensify training of physicians and to draw more doctors back into preclinical teaching and research. Facilities for the program will be housed in a new four-story addition to the Bell Medical Research Building at the Duke Medical Center. Construction will begin this summer and the first class of research students is scheduled to be admitted in July, 1959. Grants totaling $502,500 awarded for construction and equipping of the addition include: $215,000 from the National Institutes of Health, U. S. Public Health Service; $200,000 from the John and Mary R. Markle Foundation of New York; and $87,500 appropriated by the Duke University board of trustees. The faculty will include six full-time teacher-investigators who will be added to the medical center staff. The program will be geared to train some 20 students, who will integrate the research training with their regular four-year medical school curriculum; house staff physicians; and a small number of Ph.D. candidates in the preclinical sciences and nonmedical science departments. Selection will be based largely on "evidence of a research bent of an inquiring critical and original mind." Priority will be given to Duke students. Members of the planning committee include Dr. Eugene A. Stead Jr., chairman, department of medicine; Norman F. Conant, Ph.D., professor of mycology; Dr. David T. Smith, chairman, microbiology department; and Joseph E. Markee, Ph.D., chairman, anatomy department.

Personal.—The Professor Award of the University of North Carolina, Chapel Hill, was given to Dr. Hugh M. Hill, instructor in obstetrics and gynecology. This award is voted each year by the members of the senior class of the University of North Carolina School of Medicine to the professor who has contributed most to their education. The presentation was made by William Beckman of Chapel Hill, president of the class.——Dr. Arthur H. London Jr., Dr. Eugene P. Pendergrass, and Wesley C. George, Ph.D., were among six men presented Distinguished Service Awards by the University of North Carolina School of Medicine recently. The annual awards, which were presented at the banquet held in connection with Medical Alumni Day, go to persons who have made "outstanding contributions to the field of medicine or the University of North Carolina School of Medicine."

NORTH DAKOTA

New Biochemical Research Laboratory.—Bids have been approved by the North Dakota Board of Higher Education for the construction of a $200,000 biochemical research laboratory, to be located south of the University of North Dakota School of Medicine. The new laboratory was made possible by a $75,000 grant to Dr. William E. Cornatzer, head, department of biochemistry, from Mrs. Bertha Ireland, of Grand Forks, after whom the laboratory will be named; $74,190 from the National Institutes of Health grant for research facilities; and the remainder from the state medical center.

Society News.—The North Dakota Academy of General Practice has elected the following officers: Dr. Alan K. Johnson, Williston, president; Dr. David G. Jaehning, Wahpeton, vice-president; and Dr. Richard D. Nierling, Jamestown, secretary-treasurer. The next annual meeting will be held Nov. 21-22 at Grand Forks.

TENNESSEE

State Medical Election.—Officers of the Tennessee State Medical Association for 1958-1959 are: president, Dr. James C. Gardner, Nashville; president-elect, Dr. Harmon L. Monroe, Erwin; vice-president, Dr. Bergein M. Overholt, Knoxville; vice-president, Dr. Hubert P. Clemmer, Milan; vice-president, Dr. John T. Moore Jr., Algood; secretary-editor, Dr. Rudolph H. Kampmeier, Vanderbilt Hospital, Nashville; and executive secretary, Mr. J. E. Ballentine, 112 Louise Ave., Nashville 5.

VIRGINIA

Society News.—Officers of the Virginia Society of Ophthalmology and Otolaryngology for 1958-1959 are: Drs. Calvin T. Burton, Roanoke, president; Maynard P. Smith, Richmond, president-elect; William C. Anderson, Winchester, vice-president; and Marion K. Humphries Jr., 104 E. Market St., Charlottesville, secretary-treasurer.——The Virginia Society of Anesthesiologists has elected the following officers: president, Dr. Lewis E. Mangus, Alexandria; vice-president, Dr. F. Willson Daily, Roanoke; secretary-treasurer, Dr. Campbell Harris Jr., Richmond.——The Virginia Pediatric Society has elected the following officers: Dr. Harry D. Cox, Portsmouth, president; Dr. Robert H. Cox Jr., Lynchburg, vice-president; and Dr. O. Watts Booth, Newport News, secretary-treasurer.

GENERAL

Fellowships for Heart Research.—Medical research scientists are invited to submit applications for grants from the American Heart Association for support of studies in the field of heart and blood vessel diseases, Dr. George C. Griffith, president of the Los Angeles County Heart Association, has announced. Applications will be for studies to be developed during the fiscal year beginning July 1, 1959. The deadline for research fellowship applications and established investigatorships is Sept. 15. Applications for grants-in-aid must be made by Nov. 1. These grants will be made by the American Heart Association from public contributions to the Heart Fund.

Award for Urology Research.—The American Urological Association offers an annual award of $1,000 (first prize of $500, second prize $300 and third prize $200) for essays on the result of clinical or laboratory research in urology. Competition is limited to urologists who have been graduated not more than 10 years, and to hospital internes and residents doing research work in urology. The first prize essay will be read at the meeting of the American Urological Association, to be held at the Chalfonte–Haddon Hall, Atlantic City, N. J., April 20-23, 1959. For information write the Executive Secretary, William P. Dudusch, 1120 N. Charles St., Baltimore, Md. Essays must be received before Dec. 1.

Bahamas Medical Conference.—The sixth Bahamas Medical Conference will be held at the British Colonial Hotel in Nassau Nov. 28-Dec. 18. The following will be participants:

Drs. Charles H. Brown, George Crile Jr., and E. Perry McCullagh, Cleveland; Ethan A. Brown, William B. Castle, and George W. Thorn, Boston; James F. Dowd and Robert D. Woolsey, St. Louis; Helen F. Dunbar and Felix Wroblewski, New York City; George E. Farrar Jr., Richard K. Greenbank, and Marvin J. Seven, Philadelphia; Joseph F. Fazekas, Edward D. Freis, and Brig. Gen. Thomas E. Mattingly, Washington, D. C.; Irving Hirshleifer, Brooklyn; Vernon J. Kinross–Wright, Houston; Chauncey D. Leake, Ph.D., Columbus, Ohio; Alice I. Macaulay, Valhalla, N. Y.; James H. Mendel, Miami; I. Arthur Mirsky, Pittsburgh; John C. Saunders, Orangeburg, N. Y.; and Meyer Solomon, Chicago.

Special rates for participants and their families may be obtained by writing to the manager of the British Colonial Hotel. For information write Dr. B. L. Frank, 23 E. 79th St., New York 21.

New Medical Journal.—The first issue of *Diseases of the Colon & Rectum*, sponsored by the American Proctologic Society, was the January-February issue. Dr. Louis A. Buie Sr., Rochester, Minn., is the editor-in-chief, and Dr. Harry E. Bacon, Philadelphia, the executive editor. The journal will contain articles "pertaining to diseases of the colon, rectum and anal canal . . . papers devoted to basic research in metabolism, pathology, virology, radiology, and the clinical practice of medicine and surgery . . . [and] abstracts of medical literature." Members of the editorial board are: Drs. Bacon and Garnet W. Ault, Washington, D. C.; Walter A. Fansler, Minneapolis; Warren W. Green, Toledo, Ohio; Merrell O. Hines, New Orleans; A. W. Martin Marino, Brooklyn; Jerrold P. Nesselrod, Evanston, Ill.; Hyrum R. Reichmann, Salt Lake City; Stuart T. Ross, Garden City, N. Y.; Robert J. Rowe, Dallas, Texas; Robert A. Scarborough, San Francisco; and Neil W. Swinton, Boston. Annual subscription price is $12.

Grants for Orthopedic Research.—The Orthopaedic Research and Education Foundation, Chicago, has approved grants totaling more than $10,000 to the following:

Dr. Joseph M. Janes for work at Mayo Clinic, Rochester, Minn., on "Inducing Osteogenetic Sarcoma."

Dr. Donald H. O'Donoghue for work at The University of Oklahoma Medical Center, Oklahoma City, on "Histological and Clinical Analysis of the Reparative Process Taking Place in Injured Ligaments of the Knee in Dogs."

Dr. Alvira O. Sabanas for work at Northwestern University and the Armour Institute, Chicago, on "A Knee Joint Prosthesis of Teflon and Steel."

Dr. Bertram M. Kummel for work at Newark Beth Israel Hospital, Newark, N. J., on "An Evaluation of the Gallstadius Experiment."

Dr. Kirk J. Anderson for work at University of Washington School of Medicine, Seattle, on "The Effect of Particle Size of the Homogenous Bone Transplant on the Host Tissue Vascular and Inflammatory Reaction."

Dr. Charles F. Gregory for work at University of Texas Southwestern Medical School, Dallas, on "Immune Response and Inductor Capacity of Homologous Fetal Bone Transplants."

Institute for Medical Communication.—The Institute for Advancement of Medical Communication, a nonprofit organization chartered March 12 under the laws of New York State, was formed to develop ways to increase the efficiency of information exchange among medical scientists, educators, and physicians. The institute hopes to devise and test methods of disseminating medical information which promise advantages over those in use and to serve as an information center for medical organizations with communication problems. The work will be financed by grants from private foundations and agencies, private and federal, which support medical research. The charter members of the board of directors are Chauncey D. Leake, Ph.D., professor of pharmacology, College of Medicine, Ohio State University; Homer W. Smith, Sc.D., professor of physiology, New York University College of Medicine; and Dr. Irving S. Wright, professor of clinical medicine, Cornell University. Dr. Richard H. Orr, assistant editor of *Metabolism,* will serve as executive director. An advisory board is being selected. Temporary headquarters of the institute are at 37 E. 67th St., New York 21. Information may be obtained by writing Dr. Orr.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	June 21, 1958		June 22, 1957
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	..	..	1
Middle Atlantic States			
New York	1	2	4
New Jersey	..	..	..
Pennsylvania	..	..	2
East North Central States			
Ohio	..	..	4
Indiana	..	..	1
Illinois	..	1	2
Michigan	..	..	..
Wisconsin	..	..	..
West North Central States			
Minnesota	..	..	1
Iowa	..	..	2
Missouri	..	..	4
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	..	..	1
Kansas	..	1	2
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	4
District of Columbia	..	..	..
Virginia	2	2	3
West Virginia	..	1	..
North Carolina	1	3	4
South Carolina	1	1	10
Georgia	2	4	2
Florida	2	5	..
East South Central States			
Kentucky	1	1	1
Tennessee	..	..	9
Alabama	..	..	..
Mississippi	..	2	12
West South Central States			
Arkansas	..	..	6
Louisiana	1	2	4
Oklahoma	..	1	5
Texas	11	15	28
Mountain States			
Montana	..	..	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	1	1	..
New Mexico	..	1	4
Arizona	..	..	..
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	1	..
Oregon	2	8	..
California	3	9	19
Territories and Possessions			
Alaska	..	..	..
Hawaii	7	7	..
Puerto Rico	..	..	..
Total	35	63	135

Society News.—Officers elected to the American Pediatric Society are as follows: Dr. Joseph Stokes Jr., Philadelphia, president; Dr. William L. Bradford, Rochester, N. Y., vice-president; Dr. Aims C. McGuinness, Washington, D. C., secretary-treasurer; and Dr. Robert J. McKay Jr., Burlington, Vt., recorder (editor). The 1959 meetings of the society (May 6-8) and the Society for Pediatric Research (May 8-9) will be held at The Inn, Buck Hill Falls, Pa.——The American Federation for Clinical Research has installed the following officers: president, Dr. Albert I. Mendeloff, Baltimore; vice-president, Dr. William W. Stead, Gainesville, Fla.; secretary-treasurer, Dr. George E. Schreiner, Georgetown University Medical Center, Washington 7, D. C.——At the sixth annual meeting of the Association of University Radiologists the following were elected: Dr. David M. Gould, Little Rock, Ark., president; Dr. Ernest H. Wood, Chapel Hill, N. C., president-elect; and Dr. Paul A. Reimenschneider, Syracuse, N. Y., secretary-treasurer. The seventh annual meeting will be held in Atlanta, Ga., in the spring of 1959.——The New England Roentgen Ray Society has elected the following officers: president, Dr. Felix G. Fleischner, Boston; president-elect, Dr. Stanley M. Wyman, Boston; vice-president, Dr. James R. Lingley, Worcester, Mass.; treasurer, Dr. Lloyd E. Hawes, Boston; and secretary, Dr. John E. Gary, Brookline, Mass.

World Medical Association Meets in Denmark in August.—The 12th General Assembly of the World Medical Association will be held Aug. 15-20 at the Parliament House, Copenhagen, Denmark, under the patronage of His Majesty, Frederick IX, King of Denmark. The program includes the following special topics: health education of the public; problems of doctors in hospitals and polyclinics; the health team and the challenge of world unity; nuclear radiation and the health education of the public. Topics arranged for the scientific program are as follows:

The Danish Program of Cancer Control and Eradication, Prof. Dr. Jens E. Meulengracht, president, Danish Anti-Cancer Association.
Treatment to Reduce Mortality from Toxic Effects of Soporific Drugs, Dr. Alfred J. C. C. Clemmesen, chief, psychiatric department, Bispebjerg Municipal Hospital, Copenhagen.
Permanent Sequela from Malnutrition, Dr. Jorn C. H. Thaysen, medical department A, Rigshosphitalet, Copenhagen.

A medical editors' meeting under the topic, "Medical Publications as a Responsibility of the Medical Associations," is planned. Medical motion pictures will be shown at the International Film Exhibition at which Drs. Arthur L. Abel, London, England, and Malcolm R. Hill, of Los Angeles, will introduce their own pictures. Excursions, hospital and clinic visits, and a special ladies program are arranged. Registration fee is $15 for each member and $10 for each family member. For information write the World Medical Association, 10 Columbus Circle, New York 19.

FOREIGN

Microbiology Congress in Stockholm.—The 1958 meeting of the International Congress for Microbiology, under the auspices of the International Association of Microbiological Societies, will be held Aug. 4-9 at the Royal Institute of Technology, Stockholm, Sweden, with His Majesty the King of Sweden as patron. Papers will be presented at six sections under the following divisions: microbial physiology and genetics, microbial chemistry, immunology, virology, human and veterinary bacteriology, and industrial microbiology. Included will be six symposiums with the following titles and moderators:

Recombination Mechanisms in Bacteria, Joshua Lederberg, Ph.D., Madison, Wis.
Role of Protein in Nucleic Acid Synthesis and Role of Nucleic Acid in Protein Synthesis, Prof. Arne W. K. Tiselius, Uppsala, Sweden.
Tissue Specific Antibodies, Dr. Ernest Witebsky, Buffalo, N. Y.
Latent and Masked Virus Infections, Dr. Christopher H. Andrewes, London, England.
Germfree Animals, Floyd S. Daft, Ph.D., Bethesda, Md.
Continuous Culture Methods and Their Application, Delbert W. Henderson, Ph.D., Davis, Calif.

Papers will be read in English, French, or German, with no simultaneous translation. An excursion to Uppsala including a reception is planned. A scientific and trade exhibition is arranged. For information write Dr. C. G. Henden, Bakteriologiska Institutionen, Karolinska Institute, Stockholm, Sweden.

International Congress on Chest Diseases in Tokyo.—The fifth International Congress on Diseases of the Chest, sponsored by the Council on International Affairs of the American College of Chest Physicians and presented under the patronage of the Government of Japan and the Japan Science Council, will be held Sept. 7-11 in Tokyo with the Honorable Nobusuke Kishi, Prime Minister of Japan, serving as honorary president. Over 140 papers are scheduled to be presented at 14 sessions. A symposium, "Fungus Infections" will have as participants Howard W. Larsh, Ph.D., and Dr. Michael L. Furcolow, Kansas City, Kan., and Dr. William A. Winn, Springville, Calif. The program includes the following panel discussions and moderators:

Tuberculosis, Dr. Hastings H. Walker, Honolulu, Hawaii.
Cardiopulmonary Function, Dr. Noboru Kimura, Fukuoka, Japan.
Coronary Disease, Dr. John F. Briggs, St. Paul, Minn.

Benign and Malignant Tumors of the Chest, Dr. Donato G. Alarcon, Mexico City, Mexico.
Aviation Medicine, Dr. Burgess L. Gordon, Albuquerque, N. M.

Twenty-seven fireside conferences are planned. The congress banquet will be held Sept. 10 at the Tokyo Kaikan. A program of social activities is arranged. For information write Dr. Andrew L. Banyai, Council on International Affairs, American College of Chest Physicians, 112 E. Chestnut St., Chicago.

CORRECTION

Diagnostic Problem.—In the Diagnostic Problem in THE JOURNAL May 31, 1958, page 580, entitled "Fever, Cough, and Pain in Right Lower Costal Region," Dr. Daniel S. Kushner writes that the next to the last sentence should have read as follows: "From 10 to 30% of these abscesses involve the diaphragm, resulting in empyema, or pulmonary abscess, drained by a bronchus. Abscess near the lower surface of the liver may rupture into the peritoneal cavity, colon, gallbladder, or through the abdominal wall."

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral Examination.* San Francisco, Sept. 29-Oct. 3, and Phoenix, April 5-10, 1959. The 1959 written examination will be given in various locations in the United States and Canada, July 17. The final date for filing application for the 1959 written examination is six months prior to the examination. There is no filing deadline for oral examinations. Sec., Dr. Curtiss B. Hickcox, 217 Farmington Ave., Hartford 8, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Written. Several Cities,* June 30. *Oral.* Detroit, Oct. 17-19. Final date for filing all applications is April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 20, 1958. *Oral.* Chicago, Oct. 13-16. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Applications for certification, new and reopened, Part I, and requests for re-examination Part II, are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of application is September 1, 1958. No application can be accepted after that date. It should be noted by prospective candidates that the deadline Sec., Dr. Robert L. Faulkner, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: test (Part I), January 1959. Final date tion is July 1, 1958. *Oral Examinations* Chicago, Oct. 17-22. Sec., Dr. Merrill J. Cape Cottage Branch, Portland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* cago, Jan. 21-23, 1959. Deadline for receipt of applica is Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 6-10. Final date for filing application was April 30. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Chicago, Oct. 30-Nov. 1. Final date for filing application is Sept. 30. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 24-26 and New York, Dec. 5-7. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Chicago, Oct. 9-11. Final date for receipt of case reports is July 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Examination in Public Health.* St. Louis, Oct. 24-26. Final date for filing application is Aug. 15. Sec., Dr. Thomas F. Whayne, 3438 Walnut St., Philadelphia 4.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written, Parts I and II.* September 1958. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Regular Examination.* Washington, D. C., Dec. 8. Final date for filing application was July 1. *Special examination in Nuclear Medicine for those diplomates in Radiology or Therapeutic Radiology.* Washington, D. C., Dec. 6. Final date for filing application is Oct. 1. *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application is Nov. 1. Candidates completing training June 30, 1959 are not eligible for the Spring 1959 examinations. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: Written examinations (Part I) will be held at various centers in the United States, Canada, Hawaii, Puerto Rico, and certain military centers abroad on December 3. The date of the Fall examination in *Part I* has been changed from the last Wednesday of October as announced in its current Booklet of Information to December 3, 1958. Thereafter, examinations in Part I will be held once annually, on the first Wednesday of December. The closing date for filing applications will be August 1. *Part II.* Baltimore, March 10-11. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

BOARD OF THORACIC SURGERY: The fall written examination will be given in September 1958 and closing date for registration is July 1. Registration for the fall oral examination closes July 1.

AMERICAN BOARD OF UROLOGY: *Written Examination.* Twenty-five cities throughout the country, Dec. 5. The oral will be given in Chicago in February 1959. Sec., Dr. William Niles, Wishard, Jr., 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

AIR FORCE

Conference on Space Medicine.—European experts on problems of space flight have accepted invitations to a symposium on the physics and medicine of the atmosphere and space, to be held at the Hilton Hotel in San Antonio, Texas, Nov. 10-12. The international discussion will be sponsored by the U. S. Air Force School of Aviation Medicine and conducted by the Southwest Research Institute of San Antonio.

Among those from abroad who have accepted invitations are Marcel Nicolet, of the Meterological Institute of Belgium in Brussels, secretary of the worldwide organization collecting data for the International Geophysical Year, who will speak on solar radiation; Walter Dieminger, head of the Max Planck Institute for Ionosphere Research in Lindau, Germany; Jacob Eugster, University of Zurich, Switzerland, known for research on medical effects of cosmic radiation; L. R. Shepherd, London, president of the British Interplanetary Society; Gerard de Vaucouleurs, of the Astrophysical Institute of Paris, renowned for his studies of Mars; and Alberto Hurtado, director, Institute of Andean Biology in Lima, Peru.

Many distinguished American scientists have accepted invitations to the symposium, the co-chairmen of which will be Major Gen. Otis O. Benson Jr., commandant of the U. S. School of Aviation Medicine, and his advisor on space research, Dr. Hubertus Strughold.

Consultants Visit Alaska Installations.—Drs. Leroy A. Calkins of the University of Kansas Medical Center, an Air Force national consultant in obstetrics and gynecology, and Benjamin H. Balser of New York City, a national consultant in psychiatry, recently visited Air Force medical installations in Alaska, in line with the surgeon general's policy to provide advice on problem cases and conduct lectures and teaching sessions at medical installations.

Personal.—Col. Paul A. Campbell has been assigned for duty to the School of Aviation Medicine, Randolph Air Force Base, Texas, to take charge of an expanding space medicine division. This is Colonel Campbell's third assignment with the School of Aviation Medicine. The new division of space medicine which Colonel Campbell heads is an extension of the department of space medicine that Dr. Hubertus Strughold created at the school in 1949.——Col. Raymond T. Jenkins has been assigned to the surgeon general's office as Deputy Director of Plans and Hospitalization, replacing Col. Geoffrey P. Wiedeman, M.C., who is now assigned as surgeon of the Atlantic Division of the Military Air Transport Service, McGuire Air Force Base, New Jersey.

ARMY

Influenza Immunization Program Announced.—The surgeon general's office has announced that a new polyvalent influenza vaccine giving protection against Asian, Swine, A, A′, and B strains of the disease will be administered during October, 1958, to all U. S. Army personnel on active duty.

In addition to those vaccinated in October, 1958, all personnel who enter on active duty in the Army prior to Aug. 1, 1959 (including those on active duty for training for periods in excess of 30 days), will receive the vaccine. Vaccination on a voluntary basis will be offered in overseas areas to those dependents of U. S. military personnel and those civilian employees of the military services and their dependents for whom Army medical facilities have logistic responsibility.

The new vaccine will be given as a single 1-cc. subcutaneous injection to servicemen and to all others aged 13 and over. Children aged 6 through 12 may be given two subcutaneous doses of 0.5 cc. each at an interval of one week. Vaccination of children younger than 6 years is not usually recommended as a routine procedure, though if vaccination is indicated, children 3 months through 5 years may be given two 0.1 cc. doses intradermally one week apart.

Personal.—In a graduation ceremony at Brooke Army Medical Center, June 13, the Skinner Medal was presented to Capt. Clarke Turner Harding Jr., of Hillside, N. J. The Skinner Award is presented annually to the medical officer with the highest scholastic rating in each company-level course for career officers.——Col. Louis H. Jobe Jr., chief, Professional Services Division, was cited for meritorious service by the Fifth U. S. Army Surgeon, in a ceremony, June 16, at Army headquarters in Chicago. Colonel Jobe is leaving shortly for assignment as chief of the Medical Section with the U. S. Army element of the Military Assistance Group in Taiwan.

VETERANS ADMINISTRATION

Personal.—Dr. George J. Weinstein, chief, mental hygiene clinic at the VA New York City regional office, has been transferred to Washington, D. C., as chief of VA outpatient psychiatry, succeeding Dr. Raymond Feldman, who has joined the National Institutes of Health.

DEATHS

Banks, George Thomas ⊕ Fairmount, Ga.; Chattanooga (Tenn.) Medical College, 1907; physician for the Louisville and Nashville Railroad Company; died April 26, aged 80.

Beshoar, Ben B. ⊕ Trinidad, Colo.; Kansas City (Mo.) Medical College, 1903; veteran of World War I; county coroner; for many years member of the board of health of Colorado, and postmaster of Trinidad; past-president of the school board; at one time chief surgeon for the United Mine Workers; surgeon-in-chief of the Sons of Confederate Veterans; died in Denver May 1, aged 75, of shock, following an operation.

Bowles, John Herschel ⊕ Muncie, Ind.; Rush Medical College, Chicago, 1925; served as secretary of the city board of health; on the staff of the Ball Memorial Hospital; died May 3, aged 59, of fracture of the cervical spine due to a fall.

Brumback, Lynn Hamilton ⊕ Hagerstown, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1920; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; chief, department of surgery, Washington County Hospital, where he died May 7, aged 62, of acute coronary occlusion.

Cline, Gerald Morris ⊕ Bloomington, Ill.; born in Le Roy, Ill., May 31, 1896; University of Illinois College of Medicine, Chicago, 1920; clinical associate professor of pediatrics at his alma mater; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics and past-president of the Illinois chapter; fellow of the American College of Physicians; veteran of World War I; served on the advisory board of the division of handicapped children, state department of welfare, and a member of the Illinois Commission for Handicapped Children; medical director of the Illinois Soldiers' and Sailors' Children's School Hospital in Normal; associated with the St. Joseph's and Mennonite hospitals in Bloomington and Brokaw Hospital in Normal; died in Fort Lauderdale, Fla., May 17, aged 61, of coronary thrombosis.

Crump, James Emmet, Winter Haven, Fla.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1906; served as member and president of the state board of medical examiners; died in the Winter Haven Hospital April 26, aged 80, of gastric ulcer.

Darnell, Samuel Irwin, Easton, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1908; on the staffs of the Warren Hospital in Phillipsburg and the Hahnemann Hospital in Philadelphia; died May 1, aged 73, of cerebral thrombosis.

Dillon, Elmo Eugene ⊕ Homewood, Ill.; Northwestern University Medical School, Chicago, 1927; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; on the staffs of the Ingalls Memorial Hospital in Harvey and St. James Hospital in Chicago Heights; director of the Homewood Savings and Loan Association; died in the Presbyterian–St. Luke's Hospital in Chicago May 13, aged 59, of intracerebral hemorrhage.

Eaker, William Court ⊕ Alton, Ill.; St. Louis University School of Medicine, 1945; for two years served in the medical corps of the U.S. Army Reserve; associated with Wood River Township Hospital in Wood River, St. Joseph's, Alton Memorial, and St. Anthony's hospitals; died April 10, aged 43, of a self-inflicted gunshot wound of the head.

Ehrlich, Simon, New York City; Cornell University Medical College, New York City, 1902; served on the staffs of the Beth Israel, Jewish Memorial, and New York hospitals; died May 7, aged 80 of coronary occlusion.

Ely, Orriman Stewart ⊕ South St. Paul, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1906; for many years city health officer; died in the Miller Hospital April 29, aged 79, of acute cerebral edema.

Estill, Reverdy Van Warren, Charleston, S.C.; Hospital College of Medicine, Louisville, Ky., 1903; at one time assistant physician in the department of student health at Rutgers University in New Brunswick, N.J.; served on the New Jersey State Boxing Commission; died April 20, aged 81.

Everhart, Lysle Rogers, Cumberland, Md.; Jefferson Medical College of Philadelphia, 1922; died April 21, aged 60.

Fogg, Neil Augustus, Freeport, Maine; Harvard Medical School, Boston, 1916; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; veteran of World War I; formerly practiced in Rockland, where he was chief surgeon of the Knox

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⊕ Indicates Member of the American Medical Association.

County General Hospital and president of the Rotary Club; died in the Maine Medical Center, Portland, April 27, aged 68, of posterior myocardial infarction.

Fox, George Timothy, Bristol, Pa.; Jefferson Medical College of Philadelphia, 1907; an associate member of the American Medical Association; veteran of World War I; on the staff of the Lower Bucks County Hospital, where he died May 8, aged 75, of cerebral thrombosis.

Frantz, Winter Reginald ⊕ Cumberland, Md.; Johns Hopkins University School of Medicine, Baltimore, 1912; veteran of World War I; served as health officer for Allegany County, deputy health officer for Maryland, and health officer for Cumberland; died in the Good Samaritan Hospital, West Palm Beach, Fla., April 5, aged 71, of acute myocardial infarction.

Fredricks, Leonard Henry, Bismarck, N.D.; University of Minnesota Medical School, Minneapolis, 1928; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past-president of the Sixth District Medical Society; on the staffs of Bismarck and St. Alexius hospitals; one of the founders of the North Dakota Mental Health Association, of which he was vice-president and member of the board of directors; member of the staff of the Quain and Ramstad Clinic; died April 27, aged 57.

French, James Thomas, Monroe, La.; University of Tennessee College of Medicine, Memphis, 1914; member of the Louisiana State Medical Society; for many years parish coroner; on the staff of St. Francis Hospital, where he died April 22, aged 77, of coronary occlusion.

Freund, Julius Theodore, Emma, Mo.; St. Louis University School of Medicine, 1904; died April 26, aged 77, of nephritis.

Furman, Herman Charles, East Orange, N.J.; Columbia University College of Physicians and Surgeons, New York City, 1910; veteran of World War I; formerly practiced in Brooklyn, where he was on the staff of the Brooklyn Hospital; died April 29, aged 73.

Garrett, William Robert ⊕ Springhill, La.; University of Arkansas School of Medicine, Little Rock, 1936; died in the Baptist Hospital, Nashville, Tenn., March 18, aged 53.

Gilbert-Knowles, Mary, San Rafael, Calif.; Woman's Medical College of Pennsylvania, Philadelphia, 1912; an associate member of the American Medical Association; formerly practiced in Philadelphia; member of the Medical Society of the State of Pennsylvania; died April 28, aged 84, of arteriosclerosis.

Goff, Harry Louis ⊕ Captain, U.S. Navy; Jefferson Medical College of Philadelphia, 1925; entered the U.S. Navy in 1925; served during World War II and received the Bronze Star medal; died in Del Mar, Calif., April 19, aged 59, of coronary thrombosis.

Goldberg, Samuel James Sr., ⊕ New Haven, Conn.; Yale University School of Medicine, New Haven, 1907; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past-president of the New Haven County Medical Society and the New Haven Medical Society; commissioner, board of health, from 1926 to 1951; attending physician at the Grace-New Haven Community Hospital; died April 28, aged 72, of carcinoma of the lung.

Grossman, John Leonidas ⊕ Butler, Pa.; University of Pittsburgh School of Medicine, 1929; past-president of the Butler County Medical Society; president-elect of the medical staff, Butler County Memorial Hospital, where he was a member of the senior obstetrical staff, and where he died April 12, aged 54, of coronary disease.

Grossman, Louis Ward ⊕ New Castle, Pa.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1915; past-president of the Lawrence County Medical Society; veteran of World War I; associated with Jameson and New Castle hospitals; died April 18, aged 71, of lymphosarcoma.

Groves, Daniel Chester, Albuquerque, N.M.; University of Pennsylvania Department of Medicine, Philadelphia, 1903; formerly associated with the Veterans Administration Hospital; died April 24, aged 80.

Guthrie, Thomas Franklin, San Antonio, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1908; died April 28, aged 75, of myocardial infarction.

Hall, Emory Harold, Dunkirk, Ind.; Indiana University School of Medicine, Indianapolis, 1926; member of the American Academy of General Practice; veteran of World War II; died April 28, aged 58.

Harris, Maurice B.; Dallas, Texas; (licensed in Texas, under the Act of 1907); died April 20, aged 83, of cerebral anoxia and cardiac failure.

Hopwood, Lucius Locke ⊕ Colonel, U.S. Army, retired, San Antonio, Texas; born in 1879; Jefferson Medical College of Philadelphia, 1904; entered the medical department of the Army in 1905 and later graduated from the Army Medical School, the Medical Field Service School, and the Army Industrial College; served in the Philippines during the Second Pulajan Rebellion in 1906 and on the Mexican Border in 1916; during World War I, commanded Field Hospital number 2, the Pennsylvania Hospital–Columbia University unit, which was attached to the British Forces at Etretat, France; awarded the Distinguished Service Medal for his wartime service; after the war most of his service was in Washington, D.C., and included duty as executive officer, Walter Reed Army Hospital, and with the Surgeon General's office; also served as the Army surgeon in the Panama Canal Zone; retired in December, 1932, for physical disability; fellow of the American College of Surgeons, service member of the American Medical Association; died in the Brooke Army Hospital, Fort Sam Houston, April 3, aged 78, of coronary occlusion.

Howard, Arthur Bickford, Concord, N.H.; University of Vermont College of Medicine, Burlington, 1910; member of the New Hampshire Medical Society; veteran of World War I; for many years assistant superintendent of the New Hampshire State Hospital, where he died April 28, aged 71, of carcinoma of the liver.

Howell, Leslie Braden, St. Louis; Meharry Medical College, Nashville, Tenn.; 1925; served on the staffs of the Peoples Hospital and St. Mary's Infirmary; died April 1, aged 59, of hypertensive cardiovascular disease.

Johnson, John Peter ⊕ Varna, Ill.; Bennett Medical College, Chicago, 1914; served as coroner of Marshall County and as president of the high school board of directors; died April 3, aged 82.

Jordan, Patricia ⊕ Chicago; Chicago Medical School 1949; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; interned at the Macon (Ga.) Hospital and served a residency at the Elgin (Ill.) State Hospital; on the staff of Milwaukee Sanitarium Foundation; died April 28, aged 43, of coronary occlusion.

Jordan, Ray Bradley ⊕ Windsor, Mo.; University of Louisville (Ky.) School of Medicine, 1933; died in the Windsor Hospital March 17, aged 55.

Judd, Harry Weston ⊕ Mineral, Va.; North Carolina Medical College, Davidson, N.C., 1902; died in Richmond April 29, aged 77.

Keegan, Thomas Daniel, Deal, N.J.; Columbia University College of Physicians and Surgeons, New York City, 1904; an associate member of the American Medical Association; for many years president of the Hudson County Board of Health; served on the staffs of the Hudson County Contagious Disease Hospital in Secaucus, St. Francis and Margaret Hague Maternity hospitals, and the Medical Center of Jersey City, where he died April 25, aged 78, of subacute intestinal obstruction.

Kiley, Daniel Joseph Jr., North Attleboro, Mass.; Tufts College Medical School, Boston, 1912; member of the Massachusetts Medical Society; health officer; for many years member of the local board of health; served as district medical examiner; on the staff of the Sturdy Memorial Hospital, where he died April 13, aged 69, of intestinal obstruction due to adenocarcinoma of colon.

Killene, Harry Franklin ⊕ East St. Louis, Ill.; Eclectic Medical Institute, Cincinnati, 1909; for many years associated with St. Mary's and the Christian Welfare hospitals; company physician for the Illinois Central Railroad; died in St. Elizabeth's Hospital in Belleville, April 6, aged 75, of cellulitis of the face and neck secondary to carcinoma.

La Fleur, Fred Joseph, Fall River, Mass.; Kentucky School of Medicine, Louisville, 1904; served as city physician; for many years on the staff of the Fall River General Hospital; died April 20, aged 76.

Langlinais, Joseph Rousseau, Lafayette, La.; University of Louisville (Ky.) Medical Department, 1909; member of the medical staff of the Southern Pacific Railroad; died in the Lafayette Sanitarium April 21, aged 77, of cerebral hemorrhage.

Lansford, John ⊕ Redkey, Ind.; Indiana University School of Medicine, Indianapolis, 1930; veteran of World Wars I and II; served on the staff of the Ball Memorial Hospital in Muncie; died in St. Henry, Ohio, April 20, aged 64, of coronary occlusion.

Laughlin, Samuel Albert, Aberdeen, Ohio; Medical College of Ohio, Cincinnati, 1897; served on the staff of the Hayswood Hospital in Maysville, Ky.; died in Cincinnati April 16, aged 82, of coronary occlusion.

Levering, William Rogers ⊕ Stroudsburg, Pa.; Medico-Chirurgical College of Philadelphia, 1908; veteran of World War I; during World War II served on the Selective Service Board; for many years school physician; member of the Radiological Society of North America; served on the board of directors of the First Stroudsburg National Bank; associated with General Hospital of Monroe County, in East Stroudsburg; died April 22, aged 78.

Lipsky, Jacob Samuel, Detroit; Chicago College of Medicine and Surgery, 1912; for many years city physician; associated with the Receiving Hospital, where he died May 4, aged 70, of pneumonia following a gastrectomy.

Little, Archibald Alexander ⊕ Texarkana, Ark.; University of Virginia Department of Medicine, Charlottesville, 1930; member of the American Academy of Pediatrics; veteran of World War II; on the staffs of St. Michael's Hospital and Texarkana (Texas) Hospital where he died April 30, aged 55, of cerebral accident.

McConnell, James William, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1890; an associate member of the American Medical Association; member of the American

Neurological Association; served on the faculty of the Graduate School of Medicine of the University of Pennsylvania; served on the staffs of the Philadelphia General, Roxborough Memorial, and Graduate hospitals; died in Upper Darby, Pa., May 8, aged 89.

McLeod, Junius Hazel, Fayetteville, N.C.; Medical College of South Carolina, Charleston, 1926; on the staffs of the Cape Fear Valley Hospital and Highsmith Hospital, where he died April 24, aged 57, of heart failure due to second and third degree burns suffered in a fire in his home.

Mankovich, Desiderius George ⊕ Punxsutawney, Pa.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1931; secretary of the medical staff at Adrian Hospital; died in the Presbyterian Hospital, Pittsburgh, April 22, aged 51, of diabetic acidosis.

Marr, Robert McClellan ⊕ Clermont, Fla.; Tufts College Medical School, Boston, 1911; member of the Massachusetts Medical Society; formerly practiced in Westfield, Mass., where he was for many years chairman of the board of health, and on the staff of the Noble Hospital; veteran of World War I; during World War II an associate selective service medical examiner for the Westfield district; died in the Orange Memorial Hospital, Orlando, May 3, aged 76.

Mathewson, Franklin Wayne, Oakdale, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1903; an associate member of the American Medical Association; died Feb. 12, aged 83, of coronary disease.

Mathie, David Robert ⊕ Newton Falls, Ohio; University of Michigan Medical School, Ann Arbor, 1931; member of the American Academy of General Practice; past-president of the Trumbull County Medical Society; county health commissioner; associated with Trumbull Memorial Hospital and St. Joseph's Riverside Hospital, Warren, where he died April 24, aged 55, of acute pneumonitis and kidney and cardiac failure.

Miner, Elmer A. ⊕ Independence, Kan.; Northwestern University Medical School, Chicago, 1904; died in the Mercy Hospital April 25, aged 87, of adenocarcinoma of the stomach.

Nisselson, Max, New York City; Columbia University College of Physicians and Surgeons, New York City, 1905; member of the American Academy of Ophthalmology and Otolaryngology; an associate member of the American Medical Association; served on the staffs of the Lebanon and Bronx hospitals, and the Vanderbilt Clinic; died in the Polyclinic Hospital May 12, aged 84.

Ogan, Morris Lee, Ocean Grove, N.J.; Columbia University College of Physicians and Surgeons, New York City, 1903; for many years on the staff of the New York City Department of Health; served as medical chief of the Westchester Division of the New York Bell Telephone Company; died May 3, aged 88.

Paprocki, Theodore Felix ⊕ Ogdensburg, N.Y.; Long Island College of Medicine, Brooklyn, 1938; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; veteran of World War II; on the staffs of the A. Barton Hepburn Hospital and St. Lawrence State Hospital; died April 30, aged 47, of cancer.

Pauly, Michael H., Chicago; Jenner Medical College, Chicago, 1898; died in the Cook County Hospital May 5, aged 89, of arteriosclerotic heart disease and fracture of the right femur as the result of a fall.

Pertik, Otto Valentin Aloysius, Dayton, Ohio; Magyar Királyi Pázmány Petrus Tudomanyegyetem Orvosi Fakultasa, Budapest, Hungary, 1916; member of the staff of the Veterans Administration Center; died April 23, aged 64.

Polak, Isaac Benjamin ⊕ Captain, U.S. Navy, retired, San Diego, Calif.; born in Biddeford, Maine, June 27, 1894; Tufts College Medical School, Boston, 1918; while serving his internship at Waltham Hospital in Waltham, Mass., was commissioned a lieutenant (jg) in the medical corps of the Naval Reserve Force on March 16, 1918; reported for active service and subsequently transferred to the regular Navy in 1922; attained the rank of captain, medical corps, in 1942 and was placed on the retired list on Jan. 1, 1955, after completing more than 36 years of active service; commanded Naval Base Hospital number 8 during World War II; served as executive officer of the Naval hospitals at Quantico, Va., and Newport, R. I., and as commanding officer of the Naval Hospital, Memphis, Tenn.; prior to retirement was serving at a marine corps recruit depot; died April 24, aged 63, of coronary occlusion.

Prout, Charles Dusenbury, Asbury Park, N.J.; New York Homeopathic Medical College and Flower Hospital, New York City, 1915; past-president of the Monmouth County Medical Association; a physician in the Asbury Park school system for 36 years; for many years associated with the Fitkin Memorial Hospital in Neptune; died May 3, aged 69, of chronic cor pulmonale.

Pulsifer, Tappan Chase ⊕ Berlin, N.H.; Columbia University College of Physicians and Surgeons, New York City, 1899; member of the staff of St. Louis Hospital, where he died April 21, aged 88, of hypostatic pneumonia and arteriosclerosis.

Reynolds, Harry Badger, Palo Alto, Calif.; born in Woodstock, Ill., Feb. 25, 1874; Columbia University College of Physicians and Surgeons, New York City, 1900; fellow of the American College of Surgeons; served overseas during World War I; formerly associate professor of surgery at San Francisco Polyclinic and on the faculty of the University of California School of Medicine in San Francisco; served as a teacher in the liberal arts division at Stanford; one of the city's first councilmen and was a member of the high school board of education; died in the Palo Alto Hospital May 4, aged 84, of coronary occlusion.

Roberts, Walter, Berwyn, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1893; emeritus professor of otolaryngology at the University of Pennsylvania Graduate School of Medicine in Philadelphia; specialist certified by the American Board of Otolaryngology; an associate member of the American Medical Association; member of the American Laryngological, Rhinological and Otological Society; served on the staff of the Methodist Hospital in Philadelphia; died in Newton Square March 21, aged 87, of arteriosclerotic cardiovascular disease.

Root, Benjamin A., York, Neb.; Lincoln Medical College of Cotner University, 1905; an associate member of the American Medical Association; veteran of the Spanish-American War; on the staff of the York General Hospital, where he died April 4, aged 82, of cardiac failure.

Scanlan, William Dennis Jr. ⊕ New York City; Yale University School of Medicine, 1938; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; veteran of World War II; associated with North Shore Hospital in Manhasset, N. Y., St. Clare's and Roosevelt hospitals in New York City, and St. Francis Hospital and Sanatorium for Cardiac Children in Roslyn, N. Y.; died May 8, aged 46, of an overdose of barbiturates.

Shelby, Charles H., Memphis, Tenn.; Meharry Medical College, Nashville, 1901; died March 28, aged 85.

Shevell, Max ⊕ Otisville, N.Y.; University of Petrograd, Russia, 1921; member of the American College of Chest Physicians and the American Trudeau Society; on the staff of the Elizabeth A. Horton Memorial Hospital in Middletown; served on the staff of the Municipal Sanatorium; died April 22, aged 66, of coronary occlusion.

Sollars, Edward Eli, Rawlings, Md.; Maryland Medical College, Baltimore, 1910; for many years practiced in Deer Park; died April 21, aged 73, of arteriosclerotic cardiovascular disease.

Spawr, Clarence V., Benton Harbor, Mich.; Chicago College of Medicine and Surgery, 1909; veteran of World War I; died in the Mercy Hospital April 27, aged 77.

Steiner, Max ⊕ Detroit; Wayne University College of Medicine, Detroit, 1934; specialist certified by the American Board of Psychiatry and Neurology; veteran of World War II; formerly clinical director of the Pontiac (Mich.) State Hospital; died in the Grace Hospital April 29, aged 51.

Stern, Otto, Rome, Ga.; Medizinische Fakultät der Universität, Vienna, Austria, 1920; member of the American Trudeau Society; on the staff of the Battey State Hospital; died in Miami Beach, Fla., May 1, aged 64, of myocardial infarction and coronary thrombosis.

Tremblay, Julien Latance, San Francisco; St. Louis University School of Medicine, 1913; veteran of World War I; formerly associated with the Veterans Administration; died April 27, aged 73, of coronary arteriosclerosis.

Waggoner, Jonathan Elisha ⊕ Downers Grove, Ill.; Bennett Medical College, Chicago, 1902; Northwestern University Medical School, Chicago, 1904; formerly on the faculty of Bennett Medical College in Chicago; died in the Hinsdale (Ill.) Sanitarium and Hospital May 8, aged 83.

Waller, Constantine Perkins, St. Petersburg, Fla.; Vanderbilt University School of Medicine, Nashville, Tenn., 1915; served with the Veterans Administration; died in the Veterans Administration Hospital, Bay Pines, April 26, aged 73, of coronary thrombosis.

Weatherford, James Elwood ⊕ Denver; Jefferson Medical College of Philadelphia, 1915; died April 21, aged 67, of arteriosclerotic heart disease.

Weaver, John Calvin ⊕ Atlanta, Ga.; Medical Department of Tulane University of Louisiana, New Orleans, 1901; fellow of the American College of Surgeons; on the staffs of the Georgia Baptist and Crawford W. Long hospitals; served on the faculty of Emory University School of Medicine; at one time surgeon in charge of the U.S. Federal Penitentiary; died April 22, aged 79, of bronchopneumonia and chronic glomerulonephritis.

Woods, Clarendon Barron ⊕ Colonel, U.S. Army, retired, Walterboro, S.C.; Medical College of South Carolina, Charleston, 1929; also a pharmacist; entered the medical corps of the U.S. Army in July, 1933; during World War II commandant of the 185th General Hospital at Taunton, England; retired Nov. 30, 1946; service member of the American Medical Association; member of the American Academy of General Practice; served as health officer of Colleton County; chief of staff of the Colleton County Hospital; died in the U.S. Naval Hospital, Charleston, April 23, aged 57, of acute staphylococcic meningitis.

FOREIGN LETTERS

AUSTRALIA

New Medical School.—In the past, medical students of Western Australia had to study in other parts of the country, usually Adelaide, because there was no medical school in the west. This has now been remedied with the opening of a new medical school at Perth. The school was planned in 1955 by the Australian government, after an appeal for funds which raised $1,400,000. The population of Western Australia is only 700,000. Including medicine, there are now nine faculties in the University. Although the buildings have not yet been completed, the teaching of medicine began last year, when 85 students were enrolled, and 16 more, who had commenced their studies in Adelaide, returned to their home town to complete their sixth year of study. There will be no shortage of money for research, as several gifts and bequests for this purpose have been made and $700,000 of the appeal money has been set aside for this purpose.

FRANCE

Alveolar Hyperventilation Syndrome.—On the basis of 31 cases, J. Lissac (*Presse méd.* 66:740, 1958) described the alveolar hyperventilation syndrome. Although hypocapnia is often unrecognized clinically, measurement of the gases in arterial blood is particularly valuable when coupled with a study of the acid-base balance, the plasma electrolytes, and the oxyhemoglobin saturation. The first type of hypocapnia is observed in the course of disturbances of central origin—either an organic neurological disease or the use of a stimulobulbar drug or a primary hyperventilation. A second type is associated with the hypoxias; hypocapnia may be noted even though there is paralysis of the respiratory muscles when the subject has kept 20% of his vital capacity. The third type is passive hyperventilation in ill-controlled artificial respiration, and the fourth type is hyperventilation due to metabolic acidoses.

Asthma and Sex Hormones.—J. Turiaf and co-workers (*Presse méd.* 66:677, 1958) studied the possible relationship between asthma and disturbances in sex hormones. Of 565 asthmatic women, 462 were of child-bearing age; 198 became pregnant while the asthma was beginning or developing; and 103 developed asthma starting in the course of or after the menopause. Menstrual disturbances were encountered in 49.3% and premenstrual aggravation of asthma in 46%. Premenstrual increase of the asthmatic attacks was seen in 79% of those with menstrual disturbances. In the course of pregnancy, the asthma remained unchanged in 21.2%, disappeared in 40.4%, began in 19.2%, and became aggravated in 19.2%. This association may be explained by two mutually compatible concepts. The first supposes that the asthma and disturbances in sex hormones are the consequences of simultaneous but independent forces. The other holds that the hormonal disorders constitute an etiological "composant" of the asthma due to an autoallergy to sex hormones; humoroenzymatic changes with asthmogenic potency; and reactional disturbances of the major vegetative centers.

INDIA

Chronic Nonspecific Pneumonia in Children.—M. Matveyev (*Indian J. Child Health,* vol. 7, May, 1958) stated that chronic pneumonia is not a generally accepted term and that, although the condition is not rare in children, it has not been sufficiently investigated. Chronic pneumonia is a systemic disease characterized by a prolonged inflammatory involvement of the lung, with recurrent remissions and exacerbations, and should include all chronic, nonspecific, inflammatory, proliferative, and destructive involvements of the lung and bronchus. The main diagnostic distinction is between chronic pneumonia and pulmonary tuberculosis. Recurrent pneumonia and upper respiratory catarrh form the main predisposing factors, while recurrent involvement of lungs and bronchi affecting the ventilation and circulation and lowering the resistance of lung tissue lead to chronicity. The disease may assume different clinical and anatomic forms and present itself as chronic bronchitis with peribronchitis, pneumosclerosis, bronchiectasis, chronic lung abscess, and chronic pneumonia with an asthmatic syndrome. Although the clinical features are variable, the pulmonary symptoms predominate. Auscultation is more important than percussion in clinical evaluation of the condition, and roentgenography and bronchography assist greatly in diagnosing these cases. Latent respiratory deficiency is a constant feature of this disease. The course may be mild with infrequent or frequent exacerbations or rapidly progressive. In children,

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The items in these letters are contributed by regular correspondents in the various foreign countries.

various complications and intercurrent diseases add to its severity and may lead to death. Treatment is difficult. Antibiotics and tonics are used, and for the severer forms surgery may be indicated.

Tuberculoma of the Brain.—Chandy and Jadhav (*Indian J. Child Health,* vol. 7, May, 1958) reported 26 cases of tuberculoma of the brain in children. In most of them the disease was far advanced, five being totally blind on admission. Signs of increased intracranial pressure were present in all. In addition, 3 showed evidence of focal irritation, 5 had spastic hemiparesis, and 16 presented a cerebellar syndrome. In the three patients with focal seizures the lesion was in the cerebral hemisphere. The duration of symptoms varied from 15 days to 3½ years. Fever was present in 14 patients; 17 complained of loss of vision. Only 11 had obvious active tuberculous lesions in other parts of the body. The preoperative diagnosis was based on a positive tuberculin test, an increased sedimentation rate, and evidence of active or healed pulmonary tuberculosis. Spinal fluid was obtained from 10 patients at the time of ventriculography. It was normal in six, and in four there was an increase in proteins ranging from 55 to 225 mg. per 100 ml. and a moderate increase in the cell count. One patient had roentgenographic evidence of calcification. An electroencephalogram was made in two of the patients with supratentorial lesions and showed a delta rhythm in the affected region. The lesions of 19 patients were situated in the posterior cranial fossa; 4 of these were extensive, filling the whole of the fossa; 6 were midline lesions; 9 were in the cerebellum. An autopsy on one child revealed multiple tuberculomas. All patients were operated on; 14 died, 5 with postoperative tuberculous meningitis. Twelve were partially or completely relieved of symptoms.

Malignancy in Children.—In a study of malignancy in children, M. V. Sirsat (*Indian J. Child Health,* vol. 7, May, 1958) did not include those with leukemia. In the period from March, 1941, through August, 1957, 0.92% of all cancers seen at the Tata Memorial Hospital, Bombay, were in patients under 14 years of age. The most frequent sites affected by these neoplasms were the lymphatic organs, eye, bones, soft somatic tissue, adrenals, and kidneys. The age periods when these tumors were most commonly seen were the first 4 years of life and between the ages of 9 and 14 years. Retinoblastomas, neuroblastomas, and Wilms' tumors were most common in the early age period, and lymphosarcomas and bone sarcomas had the highest incidence in the older age group. Of the 260 malignant tumors in this series, only 12 were carcinomas. Of the patients with lymphosarcomas and Hodgkin's disease, 70% were boys. Soft-tissue sarcomas in children between 9 and 14 years of age were also seen more frequently in boys. The series included six cases of Wilms' tumor, four of neuroblastomas, and three of teratoma, which together are the most common retroperitoneal tumors of childhood. The 12 carcinomas included 6 lymphoepitheliomas of the nasopharynx, 3 basal cell and squamous cell carcinomas of the skin, 1 papillary adenocarcinoma of the thyroid, 1 gelatinous adenocarcinoma of the rectum, and 1 epidermoid carcinoma of the larynx.

Wax Plombage Thoracoplasty. K. K. Chaturvedi (*Indian J. Surg.* 20:1 [Feb.] 1958) stated that thoracoplasty of the modern paravertebral type has been the operation of choice in a large proportion of patients with pulmonary tuberculosis where surgery is indicated and has been found useful in arresting the disease in a number of patients. When performed in stages, the risk of the operation is minimal and complications are few. There are, however, some drawbacks to this operation, such as the resultant postoperative deformity, paradoxial movements of the diaphragm with danger of spread of the disease to the unaffected lung, the necessity of performing it in multiple stages thus increasing the cost of treatment and prolonging the stay in hospital, and the occurrence of reexpansion of the collapsed lung postoperatively in many patients, with reopening of cavities thus necessitating operation. Another method of producing collapse of the diseased lung is extrapleural pneumonolysis with various types of filling materials. This has such disadvantages as penetration of the filling material into thin-walled cavities with resultant infection, infection of the wound, pleuropulmonary fistula, and bleeding. The author combined thoracoplasty and plombage to remove the drawbacks of both forms of collapse therapy. The wax plombage thoracoplasty is performed without resection of the ribs, thus avoiding postoperative deformity. The paraffin plombe is introduced subcostally but extraperiosteally. In a series of 130 patients conventional thoracoplasty was performed on 72, ball plombage on 28, and wax plombage thoracoplasty on 30. In patients selected for operation serial roentgenograms showed a fairly well stabilized lesion with or without cavitation, and the general condition was satisfactory, with some gain in weight following conservative treatment. No patient whose serial roentgenograms showed an increase of the disease in one or both lungs was operated on. Most of the patients had had a previous trial with phrenic interruption or pneumoperitoneum. Local anesthesia, sometimes combined with intravenous anesthesia, was used for all patients.

NETHERLANDS

Retinoblastoma.—Dr. G. D. Hemmes (*Geneeskundige Bladen*, 48th series, page 211, 1958) stated that in the period July 1, 1952, to June 30, 1955, 48 new cases of retinoblastoma were reported in the Netherlands. This represents one such case in every 14,700 births, compared with one in every 34,000 25 years ago. There was also an increase in the multiple occurrence of this disease in one family. While before 1930 this seemed to be a rare occurrence, in 5 of the 47 families investigated two or more cases were found. In the present series 18 of the 48 patients had a tumor in both eyes. From a series of 23 patients investigated about 50 years ago only one had a bilateral tumor. The case fatality rate, however, is about 14%, which is much better than 50 years ago, when it was 50%. This decrease in deaths must be attributed chiefly to earlier recognition and treatment. The increase of the total morbidity could not be explained solely by a decrease in the case fatality rate. Roentgenograms of the abdomen of pregnant women may be a causative factor. In the present series, however, none of the mothers of the affected children had had any abdominal roentgenograms taken during pregnancy. On the other hand there were three cases of retinoblastoma in which one of the parents had been treated as a youth with x-rays for a retinoblastoma. In view of the increase in multiple occurrence in one family, a regular check up of the children in the affected families is urged. In the present series two cases were detected in this way. In both of these one of the parents had a retinoblastoma as a youth. In view of the increase of a bilateral tumor the children who have been treated for a retinoblastoma should be closely watched for at least four years after their final treatment of the tumor. The fact that though the incidence of the disease is increasing it is still rather rare prevents a sound evaluation of any method of treatment.

UNITED KINGDOM

Heparin for Fat Embolism.—Plasma that has become opalescent after a fatty meal is rendered translucent by heparin. Sage and Tudor (*Brit. M. J.* 1:1160, 1958) suggested therefore that the fat globules present in the blood of patients suffering from fat embolism might be similarly cleared by heparin, thereby reducing the risk of infarction. Heparin was accordingly given to three patients with fat embolism after trauma of such severity that recovery was not expected. Two patients suffered from fractures following a motorcycle injury, and another sustained fractures of the leg while playing football. When the diagnosis was made, 12,500 units of heparin was given intravenously and 0.2 Gm. of aminophylline every four hours. One patient was given 25,000 units of heparin twice daily and 0.5 Gm. of aminophylline intravenously every six hours for three days. All three patients recovered. The authors believe heparin treatment to be worthy of further trial in patients with fat embolism.

Blood Coagulation in Ischemic Heart Disease.—In view of the suggestion that the intake of dietary fat may be a determining factor in the development of ischemic heart disease, McDonald and Edgill (*Lancet* 1:996, 1958) investigated the effect of a low-fat diet on 34 patients whose blood coagulation had previously been studied. Half the patients were given a low-fat diet similar to the Kempner rice diet, and the rest were instructed to continue with their usual diet. Both groups were matched as far as possible for age and clinical condition. The thromboplastin-generation test, platelet count, prothrombin time determination (using Russell's viper venom), and estimation of platelet stickiness, blood fibrinogen, and serum cholesterol were made on all patients. Blood coagulation was measured before dieting was started, after four to five weeks on the diet, and six to seven weeks after dieting was stopped. Under the conditions of the test there was a significant decrease in platelet stickiness and in serum cholesterol after dieting, with no change in these in the control group. Estimation of platelet stickiness is a test of blood coagulability previously found by the authors to differ in patients with ischemic heart disease compared with controls and to reflect hypercoagulability. No significant difference was revealed after dieting in thromboplastin generation, blood fibrinogen, or prothrombin time.

Isolation of Trachoma Virus.—The laboratory cultivation of trachoma virus has long been attempted, but claims to success have never been confirmed, according to the WHO expert committee on the subject. Collier and Sowa (*Lancet* 1:993, 1958) took material from 10 patients in whom typical trachoma inclusions had been found. The everted lids were swabbed with 10% saline broth and the material used to inoculate 2-day, 5-day, or 6-day chick embryos. The crude yolk-sac homogenates were lyophilized in 2.5% peptone. Electron microscopy and serologic tests confirmed the presence in this material of a virus morphologically similar to that obtained from patients with trachoma. The final proof that trachoma virus was present in an active form in the yolk-sac homogenate was obtained by inoculation of the orbital sac of a blind volunteer whose eyes had been enucleated. The fornices of both eyes were rubbed firmly with a swab soaked in a 20% suspension of infected yolk-sac in saline broth. By the 7th to the 10th day conjunctival lesions resembling those seen in the early stages of trachoma appeared, and conjunctival scrapings showed the presence of typical inclusion bodies with a carbohydrate matrix. The authors believed that these observations constituted a reasonable proof of the laboratory isolation and cultivation of the trachoma virus.

Antigenic Activity of Poliomyelitis Vaccine.—The effect of a third dose of British poliomyelitis vaccine given 18 months after primary immunization with two doses was studied (*Brit. M. J.* 1:1206, 1958) in a group of 21 children who originally had no antibodies against any of the three types of poliovirus. At the time of giving the third dose, nine of the children were found to have antibody titers to a particular type that were higher than, or equal to, the corresponding titers recorded two or three weeks after the second dose. The decline in antibody titers between the second and third doses was least for type 2, which showed a fall in mean titer from 1:233 to 1:117, with none of the serums having a titer of less than 1:32 at the time of the third dose. With type 1 the mean titer fell from 1:38 to 1:7, and with type 3 from 1:66 to 1:11. With each of these types eight children had titers of 1:4 or less at the time of the third dose. The third injection of vaccine produced substantial responses to all three types. The increase in mean titer for type 1 was from 1:7 to 1:2,780, for type 2 from 1:117 to 1:17,870, and for type 3 from 1:11 to 1:7,640. The response was especially striking with type 2, in which the lowest titer after the third dose was 1:2,048. Although the responses to types 1 and 3 were not so great, no child showed a titer of less than 1:128 with either type. The results were similar to those previously reported in children who received their third dose 8 to 11 months after primary immunization.

The serologic response to poliomyelitis vaccine was also studied in 152 subjects whose ages ranged from 13 to 50 years and who, before receiving vaccine, had no antibodies against any of the three types of poliovirus. Two injections of vaccine were given at an interval of four weeks, and antibody levels were determined two weeks after the second injection. The responses to types 2 and 3 were decidedly better than that to type 1. All 152 patients had titers of 1:4 or greater to types 2 and 3, with geometric mean values of 1:148 and 1:149 respectively. With type 1, however, 12 subjects failed to show a titer of 1:4 and the geometric mean was 1:35. In general, the responses were similar to those previously reported in children aged 1 to 9 years, although there was some indication that both the older and younger groups did not respond to type 1.

Sterilization of Drugs by Irradiation.—Great progress has been made in carrying out the program of cooperative research devised to evaluate the use of radiation sources for the sterilization of pharmaceutical preparations, according to the annual report of the Association of British Pharmaceutical Industry. The results to date confirmed the earlier view that the level of radiation required to ensure sterility varies according to the organism present. Since under certain circumstances a dose of 2.5×10^{6} rad may be needed, this level of radiation has been taken as the minimum dosage to be used in the examination of various pharmaceutical preparations and chemical substances. It has also been found that a number of typical products are adversely affected by this radiation dose. Examination of other preparations indicated that this level of radiation produced no appreciable loss of potency although some change of color may occur.

Trichinosis and Butchers' Knives.—The possibility of the transmission of trichinosis by butchers' and housewives' knives was investigated by T. E. Gibson (*Ann. Trop. Med.* 52:48, 1958). Multiple incisions were made into the musculature of eight guinea-pigs heavily infested with Trichinella spiralis, and small numbers of larvas were recovered in five cases. The number of larvas recovered from the knife was: 3, 3½, 3, 1, 1. Although only a few larvas would thus appear to be likely to be transferred from even heavily infested carcasses to other food by means of butchers' knives or kitchen utensils, there is no doubt that as few as two larvas may produce infection in an animal ingesting them. It is therefore recommended that care should be taken by the butcher to cleanse his instruments between carcasses and that the housewife should pay particular attention to the cleaning of kitchen utensils used during the preparation of pork before using them on other foods.

Suicide.—Apart from India and some parts of America, England and Wales are the only countries where suicide or attempted suicide is regarded as a criminal offense. A report by a joint committee of the British Medical Association and the Magistrates Association recommended that the law of England and Wales be amended to provide that suicide and attempted suicide should no longer be a criminal offense as such. This recommendation would exclude suicide pacts and incitement to suicide. No case of attempted suicide should be brought before any court except, for example, if there is a breach of the peace. This is the practice in Scotland. It is further recommended that cases of attempted suicide which it is necessary to bring before a court should be delt with summarily as a breach of the peace. Practically all the specialists consulted by the committee agreed that the person who has attempted suicide is a case for medical and social care and that the intervention of the law is undesirable and unnecessary. In the period 1946 to 1955, 5,794 attempted suicides were brought to trial in England and Wales, 5,447 were found guilty, and 308 were imprisoned without option of a fine. The total number known to the police was 44,946. A person who attempts to commit suicide is undoubtedly in a state of mental distress and unhappiness and therefore needs special sympathy and understanding. Public opinion has moved in this direction, and it is desirable that the law should be amended in accordance with this more compassionate and merciful outlook.

Awards for Medical Research.—According to a report in the *British Medical Journal* of May 24 Sir Harold Himsworth, secretary of the Medical Research Council, appearing before the Royal Commission on Doctors' and Dentists' Remuneration in May, said that denial of distinction awards to medical research workers not having clinical responsibility was harming British medicine. Of the 500 scientifically qualified staff members employed by the council about 60% are nonmedical; these include key persons who operate complicated machines. The council has or has had research units in Africa, the Caribbean, Jordan, Egypt, and India. The council has devoted a great deal of attention to poliomyelitis vaccine, which must be tested before it is released for use. This is a great responsibility, and this responsibility is borne by the Department of Biological Standards. The present head of that department is medically qualified, but he is moving away shortly to a university. He will be succeeded by a man who is his deputy at present, who is not medically qualified. That man will have the whole responsibility for testing the poliomyelitis vaccine issued in this country. Neither of these men comes within the merit award category. In fact, of the 64 medical research workers who are Fellows of the Royal Society, 54 are ineligible for distinction awards, and of the four living British Nobel prize-winners in medicine, none are eligible. Sir Harold was asked whether such an award was not likely to cause unhappiness to those not receiving one, but he replied that he did not think so, because one of the privileges the council has been allowed to keep is that promotions are determined by merit. There is recognition on the part of the staff of the importance of merit. It should not be thought that medical research workers are a peculiarly mercenary group. They are not. Of all the branches of medicine they probably have the strongest sense of vocation. What bulked large with them was prestige.

Sir Harold was anxious about the loss of key men from this country, particularly to North America. These people receive attractive offers, and many of them Great Britain cannot afford to lose. This applies particularly to bacteriologists, geneticists, and experts on the health aspects of nuclear power. The cast of mind which makes a physiologist and that which makes an internist are similar. A person with this type of mind could go for something that led to a merit award or take up a line which carried no award. This puts an artificial distortion on a man's interest. This is one of those steadily operating factors which will not produce a crisis to jolt people into action, but we shall wake up some morning and find we have completely denuded these essential branches of medicine, a process that has already progressed too far.

Tea Break in Hospital.—The following letter from the chairman of a medical staff committee appeared in the *British Medical Journal* of May 17:

> Sir,—In common with all hospital medical staffs, we received a letter from the regional board suggesting payment for the light refreshments, cups of tea or coffee, with which we sustain ourselves. We have sent to the regional board the following letter:
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> The medical staff takes the strongest exception to this memorandum and suggestion, which represents yet another attack on long-standing tradition. The staff gives far more time and service than laid down by regulation, and feels that to be asked to pay for the small emolument represented by cups of tea is poor thanks, and a retrograde step in the continuance of cordial relations. This kind of regulation can only eventually lead to a service calculating, mean, and working to rule, and the eventual degradation of the spirit of the profession. They will not submit to this dictate.

Fingerprinting.—An expert in forensic medicine (*British Medical Journal*, May 10, 1958) expressed interest in the report that Japanese workers have developed a radioautographic method of detecting fingerprints on paper or cloth. The material left behind in a fingerprint is sweat containing minute traces of body chemicals. By this new method such materials as cloth and paper that are suspected of harboring fingerprints are exposed to a vapor of formaldehyde containing radioactive carbon atoms. The formaldehyde becomes "fixed" on the proteins of the fingerprint, and the radioactive carbon is distributed as an exact copy of the fingerprint. The treated material, after the removal of any residual formaldehyde, is then clamped to a photographic film and placed in a light-proof box in a refrigerator. Development of the radioautograph takes from one to eight days. The authors of the method claim that any latent fingerprints, except those on silk or woolen fabrics, can easily be detected in this way so long as the fingerprint protein persists. Recently, also, Davis has shown that fingerprints can be obtained by histological section to a depth of 0.6 mm. beneath the surface of the skin and suggests that this method could be used in the identification of bodies in whom the surface prints have been deliberately abraded.

To bring out a latent fingerprint on a smooth surface such as glass or a table it is necessary to make it visible for photography by outlining it with a fine powder applied with a soft brush. Various powders have been used, including aluminum, willow charcoal, lampblack, powdered graphite, and white lead. The most widely used powder, however, is made of mercury and chalk (grey powder). Mercury poisoning in police officers has undoubtedly resulted from the use of this powder, but such simple precautions as the addition of dextrose to inhibit oxidation of the mercury, the use of overalls, and the washing of hands appear to be sufficient to overcome the risks. The use of radioactive carbon will certainly raise doubts in minds conditioned by the popular press to the dangers of all forms of radiation, but radiocarbon, with a half-life measured in thousands of years, is unlikely to be any more dangerous than grey powder, though more expensive.

Royal Society of Health.—More than 2,500 delegates from 40 British Commonwealth and other countries attended the Congress of the Royal Society of Health at Eastbourne. Mr. R. Thompson, parliamentary secretary to the Ministry of Health, praised local authorities for discouraging smoking. He went on to say that in an aging population the utmost should be done to help old people stay in their own homes. The mentally ill now occupy 40% of hospital beds. Many of these could be looked after in the community with advantage to themselves and a good prospect of leading useful lives. Burning and scalding accidents in the home, which are largely avoidable, cause more than 800 deaths and 50,000 injuries a year. He concluded with the hope that adding fluoride to the water supply would be general before long.

Dr. T. P. Rees, a member of the royal commission on mental health laws, said that the mental hospital must no longer be regarded as a place where patients could be put away and forgotten. Relatively few patients in mental hospitals are dangerous. If they are locked up it is often for their own protection, but sometimes locking them up makes them become dangerous. One by one the doors of our mental hospitals have been unlocked. Hospital consultants who keep patients waiting for hours were criticized. In reply, it was claimed that, except perhaps in some large teaching hospitals, there has been a big improvement since nationalization. Physicians were urged to treat patients as human beings and to tell them what is wrong, what the chances of recovery are, and how their illness will affect their future. Greater care should be exercised, however, in discussing the patient's condition in his presence.

Sir Hugh Beaver, president of the Federation of British Industries, called attention to the intense strain to which higher executives are subject. The problem of fatigue in a manager, he said, was as vital as fatigue in an aircraft part. Desmond Curran, psychiatrist at St. George's Hospital, London, said a nagging wife or difficult foreman were often more potent causes of stress than overwork.

Physicians and midwives differed on where babies should be born. One midwife believes that the place for an Englishman to be born was in the castle of his own home, but there should be a more comprehensive home help service and more equal distribution of maternity benefits, so that the mother who had her baby at home would not be financially penalized. There should also be a nation-wide education campaign on the value of home confinement in normal cases. Another midwife said that in her area the father often acted as home helper. He likes to have his vacation when his wife is having a baby, and he runs the home very well. Mrs. Margaret Howard of the Family Planning Association commended the work of the 272 family planning clinics.

Poliomyelitis Vaccine.—There has been a major row in the House of Commons over poliomyelitis vaccine. The opposition made political capital of the shortage. The *British Medical Journal* of May 3 said that for one reason or another each of the four companies supplying the vaccine—two in Great Britain, one in Canada, and one in the United States—have had difficulty in filling their orders. Monkeys used for testing the vaccine have fallen ill, live virus was found in one batch, another batch failed to pass antigenic potency tests, and unexpected domestic demand reduced the amount of Canadian vaccine available. This was an unhappy chain of circumstances for which it is foolish to blame the Minister of Health. Where he was at fault was for not having uttered a cautionary note about supplies of a substance so fickle in its behavior during production. The Medical Research Council has agreed temporarily to forego the customary tests on vaccine from Canada and the United States.

A council spokesman said there was no question of stopping the tests on imported vaccine, but they will continue to test as rapidly as possible, and when enough has accumulated they will revert to the former policy of releasing only tested vaccine. The three types of vaccine available to health authorities are: (1) British-made vaccine, which has been tested by both the manufacturers and the Medical Research Council, (2) American vaccine at present under test in Britain, and (3) American vaccine to be imported and released without council tests. All American (including Canadian) vaccine is tested by the manufacturers and the governments in the country of origin. Physicians welcomed the Minister of Health's statement in which he made known the decision of the Medical Research Council to release untested vaccine. If the vaccine is safe for children in the United States and Canada there is no reason why it should not be equally safe for English children. The *British Medical Journal* commented that it was highly regrettable that poliomyelitis had been allowed to become a political problem. Any decision on retesting imported Salk vaccine should not be influenced by political considerations but should be made as a result of the best scientific advice available. Experts in the United States and Canada are just as capable as the British of making valid tests.

CORRESPONDENCE

INTERN MATCHING PROGRAM

To the Editor:—At the recent annual NIMP meeting, the following action was taken with regard to foreign student participation in the matching program for the 1959-1960 Intern Matching Program:

> Graduates of foreign medical schools wishing to enroll in the 1959-1960 matching program must be certified by the Educational Council for Foreign Medical Graduates. Hospitals enrolled in the National Intern Matching Program are not to offer internship appointments to nonparticipating foreign medical school graduates until after the matching program results are announced on March 16, 1959.

The foregoing is an important policy change regarding the participation of this group in the matching program.

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PARALYSIS AFTER POLIOMYELITIS VACCINATION

To the Editor:—The National Foundation for Infantile Paralysis is keenly interested in assembling all available information about paralytic disease that appears in individuals triply vaccinated against poliomyelitis. Certain cases doubtless represent failures to achieve the desired immunological response. Others, however, may be associated with infections by other enteroviruses and not by one of the three known types of poliovirus.

For the entire country, in 1957, over 200 cases of paralytic disease occurring in triply vaccinated subjects were reported as poliomyelitis. Laboratory verification of the diagnosis in many of these cases was lacking, because stool and serum specimens were not obtained or were collected too late. Accordingly, plans are being formulated to insure that during 1958 uniformly comprehensive laboratory examinations will be made in the case of all such apparent failures of the Salk vaccine.

Since chapter chairmen and state representatives of the National Foundation for Infantile Paralysis are usually among the first to learn about all new cases of paraytic poliomyelitis, an effort will be made through them to obtain specimens suitable for laboratory study. Dr. Jonas E. Salk has consented to have the necessary virus isolations and antibody titrations carried out in his own laboratory. If virus laboratory facilities are available locally, duplicate specimens should be collected for the local laboratory and for Dr. Salk.

It is important that complete laboratory studies be made on all triply vaccinated persons who suffer paralytic disease in 1958 and that practicing physicians support this important undertaking.

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BLOOD FINDINGS IN NORMAL WOMEN

To the Editor:—The paper by Judy and Price entitled "Hemoglobin Level and Red Blood Cell Count Findings in Normal Women," (*J. A. M. A.* 167:563-566 [May 31] 1958) is of great interest. Establishing normal values is an important but a very difficult task. The authors indicate that their stimulus for undertaking the study came from their frustration in attempts "to bring hemoglobin level and red blood cell count on women up to the previously established standards of 14 Gm. and of 4,800,000." This led them to question the generally accepted normal values for blood counts of women. While it is, indeed, futile to attempt to raise every patient's hemoglobin level to the average, *this is* inherent in the concept of the average and does not appear to me to be a reason to challenge the validity of the established mean.

Nonetheless, as methods improve, periodic reevaluation of the established means becomes very desirable. Such reevaluation must not rest, however, merely on the study of increased numbers of patients but rather on the use of more accurately standardized techniques and more careful selection of normal subjects. It is, therefore, disappointing to find that the authors' hemoglobin determinations have been carried out with no better standard than standardization against the photoelectric colorimeter at a local hospital. It is not stated how the photoelectric colorimeter at the local hospital was standardized. Even if the colorimeter against which the authors' was standardized was accurate, secondary standards can hardly be considered acceptable as the cornerstone for revision of norms of hemoglobin values. The instrument used should be standardized repeatedly. Standards should consist of available cyanmethemoglobin solutions or blood samples, the hemoglobin content of which has been determined by oxygen capacity or iron con-

false-positive serologic tests for syphilis, and for the unusual circulating anticoagulant of systemic lupus erythematosus. In these cases the abnormality is pinpointed by its biological activity; although specific chemical abnormalities undoubtedly exist, presently available methods are not sufficiently subtle to define them.

In conclusion, the evidence, both from the data of Jones and Thompson and from our own, is that the test described defines a nonspecific imbalance among the serum globulins, perhaps comparable to that defined by the Hanger cephalin-cholesterol flocculation. Although the Jones and Thompson test is frequently positive in patients with systemic lupus erythematosus, its specificity and sensitivity are not great enough to warrant its use as a routine diagnostic method in this disease.

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EXPERIENCE WITH USE OF GAMMA GLOBULIN IN PREVENTION OF VIRAL HEPATITIS

To the Editor:—In a previous issue of The Journal (143:631-634 [June 17] 1950) certain apparent virus hepatitis problems among persons who were engaged in working with human blood, plasma, etc., at Cutter Laboratories were discussed. In order to try and control this problem, all personnel handling blood or fractions during processing were started on a program of gamma globulin injections. This was an empirical program, and it was begun in 1949. The procedure was to inject each worker every five weeks with globulin. Initially each dose was 20 cc. This has gradually been decreased to the present dose of 10 cc. The entire program has been in effect just a few months less than nine years. The number of employees receiving globulin has varied from 50 to 75. Approximately 14 people have been on this program since its origin.

In the four years prior to the beginning of the globulin administration program there had been seven clinical cases of jaundice in people working with human blood or its derivatives in processing. Since the beginning of the program of globulin injection, no case of jaundice with or without recognizable hepatitis has occurred in this group of workers. The criteria of diagnosis have not been changed in the interim. These results suggest certain possibilities in blood transfusions, particularly where the incidence of post-transfusion infection is high.

While as yet it is not possible to say whether the previous cases of hepatitis were due to IH or SH virus, it was thought that the experience thus far should be reported. There have been no medical problems which could be traced to the injection or repeated injection of gamma globulin. Our experience has been limited to the use of gamma globulin fractionated from fresh human plasma using the Cohn alcohol technique.

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THREE GENERATIONS OF DOCTORS

To the Editor:—Frequently there are successive generations of doctors in the same family, but, as a rule, they do not practice in the home town. Often one or more practice elsewhere. With the death of my father, Dr. Raymond R. Root, on April 3, there came to an end years of continual medical service, virtually in one community, by doctors bearing the name of Root. For over 131 years there was always one doctor available by the name of Root, and for many years there were two of that name in practice at the same time.

Dr. Martin Root began practice in Byfield, a small town some 30 miles from Boston, in March, 1827. The first entry in his daybook was on March 12 of that year. The records show that his usual fee was 25 cents, treatment and medicine being provided. This statement appears in the book "The Story of Byfield," published in 1904, and there is also a statement "that the doctor's books show thousands of dollars of service rendered for which he never received any material compensation. Also for over 50 years he responded to every call by night or by day." In the book mentioned he was referred to as the Good Doctor. He died in 1880.

While Dr. Martin Root was still active, his son, Dr. Richmond B. Root, opened an office in Georgetown, their offices being only about two miles apart, so they covered virtually the same locality. He died in 1930, but while he was still active in his practice his son, Dr. Raymond R. Root, also opened an office in Georgetown and practiced until shortly before his recent death.

So the three Root doctors practiced their profession for a little over 131 years in virtually the same town.

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fever cells"), separated the patients with glandular fever into 2 groups with possibly distinct disease states. These groups were the seronegative and the seropositive, distinguishable as regards onset, symptoms, and clinical signs only in retrospect; the seropositive cases tended to be the more severe.

There were notable differences in the seasonal trends and in the age and sex incidence of the 2 disease states. The patients with a positive reaction to the Paul-Bunnell test showed a rapid increase in incidence between the ages of 20 and 29 years, followed by a rapid fall, and the patients with a negative reaction to the test and positive hematological findings showed the highest incidence up to the age of 9 years, with a steady fall thereafter. The sex distribution among the patients with a positive reaction to the Paul-Bunnell test was equal for males and females, but males predominated in a ratio of 2:1 among those with a negative reaction to the test. There was an increase in incidence in the months of April to June among the patients with a positive reaction to the Paul-Bunnell test, but there were no regular seasonal changes, although occasional peaks were observed, among those with a negative reaction. The infectivity of either disease state was low, but the seronegative disease appeared to be the more infectious. A positive reaction to the Paul-Bunnell test was found approximately twice as long as glandular fever cells were observed in the peripheral blood; a doubtful positive reaction to the test, too weak to titrate, was found to be significant and was associated either with an incipient phase or, more usually, with a regressive phase of the seropositive disease. In seropositive patients the glandular fever cells were present in significant numbers in the peripheral blood about twice as long as in seronegative patients.

Studies in Peripheral Arterial Occlusive Disease: III. Acute Arterial Occlusion.

S. Wessler, S. G. Sheps, M. Gilbert and M. C. Sheps. *Circulation* **17:** 512-525 (April) [Part 1] 1958 [New York].

This study of acute peripheral arterial occlusion was based on material obtained from 5 sources: (1) clinical information from 75 patients hospitalized with acute arterial occlusion of a lower extremity; (2) pathological examination by a special injection and dissection technique of 105 legs amputated for vascular or nonvascular disease; (3) arteriographic observations on the lower limbs of 52 cadavers; (4) autopsy studies of 9 patients who died in the hospital after acute occlusion of a leg artery; and (5) data from an experimental investigation of acute femoral artery embolism in 30 dogs. Eighty-eight per cent of the patients had clinically recognized heart disease. During the initial hospitalization 64% of the patients survived without a major amputation, 15% survived with a major amputation, and 21% died (almost one-third in the first 24 hours). Among 56 survivors on whom follow-up information was available, the 5-year survival rate was 46% compared with 82% in a New England population of comparable age, sex, and race.

Fresh occlusions were found in one-half of all legs amputated for arterial insufficiency and studied by the injection and dissection technique. In each amputated limb in which fresh arterial occlusions were found, propagation of clot was observed either distal to the most proximal clot in the extremity or distal to old occlusions or narrowing; the clots were multiple in 70% of the legs with fresh occlusions. In only 5% of the legs amputated for arterial insufficiency were fresh occlusions present without concomitant old occlusion, and in each such instance the fresh occlusion was more than 22 cm. in length and was present at the level of amputation. The clinical diagnosis of acute arterial occlusion was suspected in less than half of the patients in whose amputated legs fresh occlusions were demonstrated after injection and dissection of the extremity. The clinical diagnosis of acute peripheral arterial occlusion was related to the total length of the fresh occlusions. If the fresh occlusions exceeded 10 cm. in length in the resected specimen, the diagnosis was made in 94% of instances; if the fresh occlusions were less than 5 cm. in length, the diagnosis was made in only 10% of instances. Clinical, pathological, and experimental observations showed that clot fragmentation, clot lysis, and preformed interarterial anastomoses can compensate immediately for an acute arterial occlusion. Further increase in blood flow can occur within days to weeks after an acute occlusion through the gradual hypertrophy of anastomotic vessels that bypass occluded arteries. The autopsy material confirmed the high incidence of cardiac disease and recurrent thromboembolism.

Acute occlusion of a leg artery usually reflects but 1 episode punctuating a recurrent process having its origin in the heart. It represents a medical emergency in which the threat to life is at least as great as the threat to limb. Thus, any diagnostic or therapeutic procedure that is designed to save a limb but that increases the risk to life is not justified. It is neither feasible nor necessary to distinguish between acute arterial embolism and thrombosis. Many acute occlusions, although not recognized clinically because of their small size, may nevertheless contribute to ischemia by their strategic location or by serving as a nidus for the propagation of clot. Embolectomy, when considered in relation to the total clinical problem, is not recommended as the treatment of choice in the acute phase of the occlusive process, although its efficacy in individual cases is well documented. Evidence is inadequate to justify medical or surgical alterations in autonomic tone in the treatment of organic arterial obstruction. Fibrinolytic agents may have a place in the early treatment of acute arterial occlusion, and bypass grafting may be of value in the management of residual ischemia. The role of drugs in preserving or producing a normal sinus rhythm and of remedial cardiac surgery in diminishing the recurrence of systemic arterial emboli remains to be evaluated. Anticoagulant therapy, although not ideal, appears to offer promise of the greatest over-all benefit with the least risk.

Systemic Lupus Erythematosus: A Complex Auto-Immune Disorder? W. Dameshek. Ann. Int. Med. 48:707-730 (April) 1958 [Lancaster, Pa.].

The author reports on 11 female patients, between the ages of 10 and 61 years, with various hematological abnormalities. Four of the 11 patients had "idiopathic" thrombocytopenic purpura, 3 had autoimmune hemolytic anemia, 2 had autoimmune hemolytic anemia and "idiopathic" thrombocytopenic purpura, 1 had a positive reaction to the serologic test for syphilis and pronounced leukopenia and neutropenia, and 1 had a hemorrhagic disorder due to circulating anticoagulants. The hematological abnormalities observed in these patients with systemic lupus erythematosus may be said to be just as representative of the disease as are the "onionskin" vascular lesions of lupus erythematosus in the small blood vessels of the removed spleen, the "wire-loop" lesions in the kidneys, or the vascular and "collagen" lesions elsewhere in the body. The various hematological abnormalities, including the L. E. factor, may be considered as "autoimmune" in nature with the development of autoantibodies against various antigens in the blood cells or plasma. The L. E. factor is probably an abnormal autoantibody directed against a constituent of the leukocyte nucleus. Other leukocytic antibodies may also occur in the course of the disease. If the various hematological lesions of systemic lupus erythematosus are considered to be "autoimmune," it is likewise possible that the vascular lesions (vasculitis), with resultant skin lesions (lupus), arthritis, nephritis, pleuritis, and endocarditis, may also be due to autoantibodies, but in this case directed against small blood vessels. The entire disease of systemic lupus erythematosus thus may be a complex of immunological disturbances affecting (1) blood cells and other blood constituents and (2) small blood vessels. The L. E. factor may be considered as only 1 of the immunological abnormalities of lupus; thus, its lack in a given patient does not necessarily rule out the presence of the disease.

In several of the patients in whom systemic lupus erythematosus was associated with thrombocytopenic purpura, the latter condition was a prodrome of the systemic lupus and, consequently, every case of idiopathic thrombocytopenic purpura in a young woman should be suspected of being lupus erythematosus. "Idiopathic" thrombocytopenic purpura need not be considered to be symptomatic of lupus, but simply as 1 part of the generalized disease. Combinations of idiopathic thrombocytopenic purpura with autoimmune hemolytic anemia are even more likely to be cases of lupus, whether other manifestations of systemic lupus are present. Dissemination of the lupus process may be accelerated by splenectomy. The presence of complex mixtures of autoantibodies in systemic lupus erythematosus suggests that numerous antigens (perhaps altered blood cells, altered blood plasma constituents, or altered small blood vessels) are concerned. Since most of the patients with this disease are women, the possibility is present that development of antigen may take place in the menstruating endometrium. Here, at monthly intervals, alterations in blood cells, blood plasma constituents, and small blood vessels (spiral arteries) take place. In certain women these altered cells, plasma factors, and blood vessel constituents become autoantigenic, thus leading to the formation of several types of autoantibodies against both blood constituents and small blood vessels, and thus to the complex disease known as systemic lupus erythematosus. The periodic character of the menstrual cycle might well aid in autoantibody formation. Such a concept does not preclude the possibility of autoimmunization by other mechanisms, as in the relatively uncommon cases in male patients.

SURGERY

Functional Investigations After Pulmonary Resections or Collapse Therapy in Tuberculous Children and Adolescents. H. D. Renovanz and A. F. Riebel. Chirurg 29:172-178 (April) 1958 (In German) [Berlin].

There is no doubt that the exclusion of the tuberculous process by means of collapse therapy or pulmonary resections is of value also in children. However, functional tests over prolonged periods are necessary to decide whether, although tuberculosis is controlled by these measures, functional impairment of the respiratory and circulatory system is excessive. In this paper the authors are concerned with electrocardiographic, phonocardiographic, and spirographic studies on 51 children and adolescents who underwent resections and 25 pneumonolyses to effect collapse. From 6 months to 8 years had elapsed since these interventions. It was found that electrocardiographic changes were less frequent in children and adolescents than in adults. Phonocardiographic studies revealed increased pressure in the lesser circulation; this was indicated by a predominance of the second sound. Occasionally, accidental murmurs could be heard as the result of adhesions and of traction on the large vessels and on the heart. Respiratory studies revealed that this function was not better in children and adolescents than it was in adults after pulmonary operations. The poorest results were obtained when postoperative adhesions were present, but poor functional results were observed also after prolonged collapse therapy.

Apparently, children and young persons achieve a more adequate compensation for an estimated insufficiency than is the case in adults. This better compensation is not necessarily spirometrically demonstrable. Comparative studies on unilateral and balateral pneumothorax therapy revealed that the functional impairments with these forms of collapse therapy are not essentially different from those resulting from surgical measures. Thoracoplasty gives the poorest functional results. Decortication does not completely restore pulmonary function, because after prolonged collapse therapy the ventilatory function of the lung has become permanently impaired. Additional control studies, particularly of the cardiovascular system, will be necessary to ascertain whether persons who have been operated on during childhood or adolescence will be more subject to cardiac and circulatory failures than is the case in those undergoing pulmonary surgery at more advanced ages. Nevertheless, because of the longer life expectancy of young persons, the presence of an increased pressure in the lesser circulation, which was revealed by phonocardiographic studies, might lead to premature failure of the cardiovascular apparatus. This possibility is not completely ruled out, even though the electrocardiographic changes are less pronounced in young persons than in adults after pulmonary surgery. It is suggested that collapse and resectional therapy should not be too extensive during childhood and adolescence. The expected advantages of removing the tuberculous focus should be evaluated against the possibility of functional impairment.

Importance and Limitations of Pallidal Surgery for the Treatment of Parkinsonian Syndromes. J. Cambier. Presse méd. 66:602-604 (April 5) 1958 (In *French*) [*Paris*].

Earlier methods of surgical treatment designed to alleviate the symptoms of Parkinson's disease have now given way to operations directed toward the gray nuclei and, more particularly, the globus pallidus. The first efforts in this direction, made 18 years ago, showed that severance of the pallidofugal fibers was effective but that it required a particularly severe operation involving the penetration of the third ventricle and the creation of a hypothalamic lesion. It was, therefore, considered too hazardous for the treatment of Parkinsonian syndromes. This condition was changed with the introduction of new techniques which made it possible to interrupt the extrapyramidal pathways by electrocoagulation of the pallidum through a trephine hole. Many surgeons have since turned their attention to this problem, and, although they all have the same end in view, several have worked out their own methods of approaching the pallidal region and of creating a limited lesion. The statistics are still inadequate for any comparison between these methods. Certain fundamental principles that must be respected, whatever the method used, are: (1) the need for creating, with precision, a limited and localized lesion in a region of the nervous system that lies deep within the hemisphere and is surrounded by structures the preservation of which is essential; (2) the need for limiting the operative trauma as much as possible because of the particular fragility of the terrain; and (3) the need for carrying out the procedure, as far as possible, on a conscious subject, so that the results obtained can be evaluated during the operation. Electrocoagulation is used by almost all French neurosurgeons, but other procedures, notably the injection of alcohol or some similar substance, have also been used successfully.

The effect of the operation, which involves only a minimum of risk, is chiefly to reduce rigidity and tremor on the contralateral side. Other symptoms of the disease, especially akinesia, are less clearly influenced. Physiological senility, evidences of cerebral arteriosclerosis with a pseudobulbar state, significant vegetative disturbances, especially of a respiratory character, and the presence either of permanent psychic disturbances indicating intellectual impairment, or of serious neurotic disturbances of an anxious or obsessional type are definite contraindications to operation. The state of depression habitually found in patients with Parkinson's disease, on the other hand, is not necessarily a contraindication; in fact, operation is often followed by an improvement in the psychic condition of the patients that is out of proportion to the objective improvement in their neurological status. A unilateral operation on the side more severely affected is usually sufficient, but a bilateral operation, although slightly more hazardous, is fully justified in certain cases.

The long-term prognosis is closely linked to the progressive character of Parkinson's disease. Rigidity and tremor may reappear, usually in an attenuated form, shortly after the operation, but if the improvement secured by the operation lasts for 3 or 4 months, it can generally be regarded as stable. Recurrences, in any case, can be treated by a second operation. It must be remembered, however, th the neurosurgical treatment of Parkinson's disea is palliative only, and that the alleviation of rigidi and tremor, important as it is, does not constit a cure.

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Pallidotomy in Treatment of Parkinson's Disease. J. Sánchez Juan. Rev. clín. españ. 68:155-160 (Feb. 15) 1958 (In Spanish) [Madrid].

Pallidotomy was performed on 17 patients with Parkinson's disease. Obrador's technique was employed. The patients were between the ages of 40 and 65 years. The duration of the disease varied between 6 months and 24 years. The disease was presenile in 7 patients, had followed encephalitis in 4, was of syphilitic origin in 3, and was of unknown origin in 4. The treatment was given only to patients in good general condition and to those without fibromuscular, articular, or neurological disease, with the exception of 1 patient with kyphosis and rigidity of the thorax. The operation was performed in 2 stages. The first stage consisted of trephining of a small orifice at the temporal region (either unilateral or bilateral) with the patient under local anesthesia, and the taking of an anteroposterior and a lateral pneumoencephalogram. The trephined orifice was located 3.5 cm. above the zygomatic process on the orbital line and 1 cm. in front of the biauricular plane. The cannula reached the globus pallidus 4.5 cm. below the cerebral cortex. The second stage was carried out 2 to 5 days after the pneumoencephalography. Injections of 0.2-0.5 cc. of a 2% Novocain solution were given, and a pallidotomy was performed with Obrador's pallidotome. This instrument is provided with a needle for the injection of the Novocain solution and a steel loop wire for the production of the subcortical lesion. Excellent immediate results were obtained in 7 patients (disappearance of rigidity, tremor, spasm, and motor disorders). Good results were obtained in 6 patients (great diminution of both rigidity and tremor). The treatment failed in 4 patients. The patient with kyphosis and rigidity of the thorax obtained a great improvement which lasted 6 days, after which she presented symptoms of atelactasis of the left lung, collapse, and death. The author concludes that instrumental pallidotomy is a simple operation and gives better results than other techniques employed in chemical destruction of the globus pallidus.

Postpericardiotomy Syndrome Following Surgery for Nonrheumatic Heart Disease. T. Ito, M. A. Engle and H. P. Goldberg. Circulation 17:549-556 (April) [Part 1] 1958 [New York].

Widespread intracardiac surgery for patients with rheumatic heart disease has brought to medical attention a puzzling postoperative complication, usually designated the "postcommissurotomy syndrome" and often considered to represent reactivation of rheumatic fever. The authors present hiseryies of patients in whom an identical complication peniloped after intrapericardial surgery for con- of the sy:art disease. The syndrome was observed in 13 of 24 patients who underwent cardiac surgery that involved opening the pericardium. It developed after transventricular and transarterial valvoplasty for pulmonary stenosis, closure of septal defects, and exploration of the pericardium for inoperable congenital cardiac lesions. Although other factors may be important in the pathogenesis of this condition, the feature common to these operations on nonrheumatic as well as rheumatic patients was wide incision of the pericardium. This postoperative complication was not noted after other operations for congenital heart disease wherein the pericardium was not disturbed, nor was it found in patients in whom a small segment of pericardium was clamped to permit removal of the pericardial cyst.

Since the condition appeared after pericardial incision, with or without cardiotomy or valvotomy, the term "postpericardiotomy syndrome" is suggested as more universally applicable for this postoperative complication. The syndrome is interpreted as a traumatic pericarditis, possibly a reaction to blood in the pericardial sac. The occurrence of this postoperative manifestation in nonrheumatic subjects is a compelling argument against the concept that the syndrome in patients with mitral valvotomy usually represents reactivation of rheumatic fever.

The Treatment of Parotid Tumours in the Light of a Pathological Study of Parotidectomy Material. D. H. Patey and A. C. Thackray. Brit. J. Surg. 45:477-487 (March) 1958 [Bristol, England].

The authors adopted the policy of early exploration of parotid tumors with a view to parotidectomy. The standard operation was conservative parotidectomy, with conservation of the facial nerve. This was carried out in 68 of the 80 patients. In 6 of these the parotidectomy was partial, in 38 superfacial, and in 24 total. In 4 further cases conservation of the facial nerve was only partial. In 7 cases radical parotidectomy was carried out, with complete sacrifice of the facial nerve. The remaining patient required skin excision only for recurrence limited to the scar. Special methods of study included (*a*) complete serial sectioning of glands and their contained tumors and (*b*) "experimental enucleation" of encapsulated tumors from parotidectomy specimens, and examination of the tumor bed and of washings of the tumor surface. It appeared that the 2 factors responsible for recurrence of primary mixed tumors after enucleation are the leaving behind of peripheral nodules and implantation. No evidence was found that multiplicity of tumor foci is a factor.

The authors describe a method of growth of primary mixed tumors by phases of "focal infiltration." This feature is common in small tumors and explains the special frequency of recurrence after enucleation of small and early tumors noted by

McFarland, a finding which hitherto appeared anomalous. Recurrent *mixed* tumors are, as a rule, multiple, and implantation in the scar of the original incision is a common finding. Cylindromas and mucoepidermoid tumors are characteristically infiltrating tumors. Adenolymphomas are usually multiple and often bilateral. This multiplicity is the probable cause of the not infrequent recurrence noted after enucleation. Carcinoma is frequently superimposed on an inactive tumor of many years' duration. Developed carcinomas tend to be highly malignant. An accurate diagnosis of the nature of a parotid tumor is usually impossible clinically. Preoperative biopsy of parotid tumors is, in general, undesirable as encouraging spread, and operative biopsy should be reserved for special cases. Parotid tumors are all best regarded and treated as malignant, or potentially malignant, and operated on early. The best treatment for most parotid tumors is some form of conservative parotidectomy, i. e., parotidectomy with preservation of the facial nerve, but for infiltrating tumors resection or partial resection of the facial nerve may occasionally be necessary. The exact procedure indicated can only be determined after wide operative exposure.

Aneurysms of the Abdominal Aorta. C. Dubost and F. Chaubin. Arch. mal. coeur 51:172-183 (Feb.) 1958 (In French) [Paris].

Aneurysms of the abdominal aorta are almost always due to atheroma; cases due to syphilis are exceptional. Surgical exploration is indicated in virtually all cases because a radical cure is often possible. The technique of excision, followed by replacement of the excised segment with a graft, first successfully carried out by the authors on March 29, 1951, has been standardized, and the results that can be obtained fully justify the procedure. The diagnosis is often delayed, because the symptoms are not always clear but may resemble those caused by other conditions. Simple roentgenograms may provide useful information by showing the whole extent of the tumor, the calcareous ring around the sac, and calcified plaques in the vascular wall. Preoperative aortography is not necessary if the diagnosis is clear. It can, however, be used to obtain fairly exact information concerning the seat of the aneurysm, but it must be carried out with precision if it is to be free from danger. The exact limits of the aneurysm can only be determined at operation, because the extent to which the aorta is involved above and below the aneurysmal sac cannot be seen in the films even when a contrast medium is used. Postoperative aortography is useful as a means of evaluating the quality and the permeability of a graft.

The preoperative investigation of the patient should be exceptionally thorough, with comprehensive blood studies and careful assessment of the renal and cardiovascular status. Surgical exploration is almost invariably indicated, because (1) the survival period for patients with aneurysms of the abdominal aorta is comparatively short, even when they are asymptomatic; (2) age is not a contraindication to operation, and neither is hypertension, unless it is associated with severe cerebral and vascular complications; and (3) a history of past coronary disturbances, although common in these patients, does not justify abstention from surgery. The only definite contraindications are myocardial damage with heart failure, renal damage with azotemia, and a highly precarious general condition. The operation, in cases amenable to surgery, consists of resection of the aneurysm and the restoration of vascular continuity with a graft, which may be either human or synthetic. Human grafts obtained from young subjects afford the greatest measure of security at the present time, but synthetic grafts, because of the ease with which they can be fabricated and stored, seem to be the prostheses of the future. Resection brings up the problem of clamping above and below the aneurysm while the excision is being carried out and the necessary anastomoses are being made. The consequences of the clamping and the surgical technique, described in detail in the original article, depend on whether the aneurysm is subrenal—the commoner type—or subdiaphragmatic. The authors' personal statistics cover 16 patients treated by excision and grafting since 1951. Three patients died, 1 during operation as the result of a tear in the vena cava, 1 on the 15th postoperative day as the result of a massive pulmonary embolism, and 1 in the 2nd month after operation as the result of rupture and hemorrhage due to the elimination of an Ivalon graft. The results in the other 13 patients, 11 of whom have lately been seen at follow-up, were excellent; some of the patients have even gone back to work.

Simultaneous Primary Resection and Thoracoplasty for Pulmonary Tuberculosis: A Review of 87 Cases. A. Stranahan, T. S. Reeve, R. D. Alley and others. New York J. Med. 58:1297-1300 (April 15) 1958 [New York].

The authors report on 40 male and 47 female patients with pulmonary tuberculosis who underwent primary pulmonary resection with simultaneous modified thoracoplasty and who were studied postoperatively. Three patients had a pneumonectomy, 32 had a right upper lobectomy, 30 had a right upper lobectomy and resection of other segments, 11 had a left upper lobectomy, 4 had a left upper lobectomy and resection of other segments, 6 had a segmental resection, and 1 had a wedge resection. Thoracoplasty was felt to be necessary in only 7 patients on whom a less extensive resection than lobectomy was performed, because in most of the patients the remaining lung adequately filled the space after the resection. Most of the patients were in the 3rd and 4th decades of life. Patients, aged less than 30 years, rarely require thoracoplasty, since the young elastic lung readily fills the space after resection. The modified thoracoplasty consisted of excision of the second and third ribs subperiosteally to the transverse processes of the vertebra. By limiting this resection to relatively short posterior segments, excessive paradoxical motion of the anterior chest wall was prevented. Severe postoperative complications occurred in 3 patients; 1 of these had a severe hemorrhage the evening after the operation, which was controlled by ligation of a bleeding intercostal artery; the second patient had a nontuberculous empyema requiring thoracotomy drainage; and a bronchopleural fistula with tuberculous empyema occurred in the third patient, which was resolved by pneumonectomy. None of the 87 patients died in the postoperative period, and all were alive at the time of a recent follow-up examination. None of the patients had spread or reactivation of their disease. Sputum remained or became negative within 1 month of the resection in 82 (94%) of the 87 patients.

These data show that the combined surgical procedure was tolerated well and carried a low morbidity. By eliminating a second-stage operation, the patients were not only benefited economically but were also spared the psychological trauma of multiple surgical procedures. The decision to perform a simultaneous thoracoplasty on patients undergoing resection was based on such factors as the extent of resection, preoperative pulmonary function tests, observed elasticity of the remaining lung tissue, and general condition of the patient. Carefully modified thoracoplasty is free of many of the objections cited by other workers and obtains a satisfactory space-filling defect. Objections to the double procedure are not substantiated by the authors' results, which show that this combined operation is a valuable procedure in the treatment of patients with pulmonary tuberculosis, and in selected cases it is held to be the procedure of choice.

An Analysis of Adult Skeletal Tuberculosis. E. M. LaFond. J. Bone & Joint Surg. 40A:346-364 (April) 1958 [Boston].

Of 143 men and 87 women with proved active skeletal tuberculosis who were admitted to the Glen Lake Sanatorium in Oak Terrace, Minn., between 1928 and 1946 before streptomycin and the other new antituberculosis drugs were available, 4 were lost to follow-up and 226 were followed to Jan. 1, 1953. Sixty men (42%) were aged less than 34 years, and 53 (37%) were between 35 and 40 years. The commonest sites of location of tuberculosis were the major weight-bearing joints, especially in the axial skeleton. The lesions were usually of advanced extent and were often associated with other tuberculosis conditions, especially pulmonary tuberculosis, other skeletal foci of tuberculosis, and genitourinary tuberculosis; some patients had a history of pleural effusion, of abscesses, and of sinus drainage. During the 6-to-25-year follow-up period 106 patients died of tuberculosis and 25 died of other causes, a total mortality rate of 57%. Of 148 patients who left the sanatorium alive, 57 (39%) had relapses. Among the factors which proved to be statistically significant in relation to an increased mortality rate were the location of the lesion in the sacroiliac joints, the extent of the lesion, the presence of multiple skeletal foci, and the presence of pulmonary tuberculosis.

An attempt was made to determine what effect, if any, streptomycin had on tuberculous osteomyelitis by comparing the results obtained in the 230 patients in this series with those in 196 patients with skeletal tuberculosis treated with streptomycin at Veterans Administration hospitals and in a smaller series of 21 patients treated with streptomycin at the Glen Lake Sanatorium between 1947 and 1952. Among the patients not treated with streptomycin, those with minimal lesions showed the most favorable healing or the shortest time of healing (8.7 months). The result of streptomycin treatment in all the patients receiving this antibiotic was to convert their more severe lesions to minimal lesions. The effect of streptomycin on the osseous component of tuberculosis is slight but definite.

Acute Appendicitis. J. A. Campbell and D. C. McPhail. Brit. M. J. 1:852-855 (April 12) 1958 [London].

The authors report on 243 male and 306 female patients, between the ages of 12 and more than 60 years, who were admitted to the Royal Infirmary of Edinburgh with a diagnosis of acute appendicitis that was confirmed on surgical intervention. Of the 549 patients, 352 (62%) were aged less than 30 years, and only 29 (5%) were aged 60 years or over. No patient was treated conservatively. In 441 patients (80.3%), the operation was carried out before the infection had spread beyond the appendix, but in the remaining 108 (19.7%), drainage of the area was necessary. It was found that the incidence of complicated appendicitis increased in the patients of advanced age, and that this was not solely due to delay in diagnosis but also to the more fulminating process in these patients. The classic textbook description of appendicitis was not often met with, and the incidence of atypical cases was high. It is important to suspect appendicitis in all patients with abdominal pain irrespective of age. The characteristic breath fetor and furred tongue were present in 284 (64.5%) of the 441 patients and in 106 (98.1%) of the 108 patients; if associated with much vomiting or diarrhea, these signs suggested that the infection had already spread beyond the appendix. Local tenderness over the inflamed appendix, usually in the right quadrant of the abdomen, proved to be the most important sign; it may even be the only sign, but, on the other hand, it may be absent in the very obese patients or in those of advanced age. No reliance should be placed on the pulse rate or the temperature for the early diagnosis of appendicitis. If there is a rise of temperature in the patient of advanced age, the infection has almost certainly spread beyond the appendix.

Six of the 549 patients died, an over-all mortality rate of 1.08%. Only 1 of the 441 patients in whom the infection was confined to the appendix died, a mortality rate of 0.23%. The other 5 patients who died belonged to a group of 44 patients with generalized peritonitis, which contributed to the fatal outcome. None of the 39 patients with perforated appendicitis with abscess formation died, despite the fact that the number of patients in this group was almost the same as the number with generalized peritonitis. If the operation is carried out while the infection is confined to the appendix, the mortality is at the irreducible minimum for any surgical procedure. In patients in whom the appendicitis has progressed to abscess formation, it is safer to operate and to drain the abscess. If the appendix presents, it should be removed, but if appendectomy is difficult and would require some dissection, the abscess should be drained. Early diagnosis and prompt surgical treatment are still the most important principles in dealing with this, the most common surgical emergency.

Mucormycosis of the Bronchus Successfully Treated by Lobectomy. M. L. Dillon, W. C. Sealy and B. F. Fetter. J. Thoracic Surg. 35:464-468 (April) 1958 [St. Louis].

The authors report on a 20-year-old woman with diabetes mellitus of 5-year duration, the second patient in whom the diagnosis of mucormycosis was made during life. She had suffered attacks of diabetic coma and acidosis. A chest roentgenogram taken the day of admission showed consolidation of the lower field of the right lung. During the first week in the hospital, her diabetes was well controlled, and she began coughing up foul-smelling, purulent sputum. Fluoroscopy revealed an air-fluid level in the right lower lung field which persisted for 30 days without change. Bronchoscopy on the 5th and 12th hospital days revealed granulation tissue obstructing the distal portion of the bronchus intermedius. Biopsies of specimens from the area showed chronic inflammation of the wall of the bronchus. The surface was covered by a layer of necrotic tissue and fibrinopurulent exudate, in which one could see many broad, irregular, nonseptate hyphae, which were basophilic and readily visible in routinely stained tissue. After the second bronchoscopy, the patient's condition became worse, with daily elevations of temperature ranging from 38 C (100.4 F) to 39 C (102.2 F). On the 30th hospital day a lobectomy was performed on the middle and lower lobes of the right lung with the aid of general anesthesia. The patient did well and became afebrile on the 7th postoperative day. Serial exposures after the operation showed the left lung and the upper lobe of the right lung to be expanded well. Gross examination of the surgical specimen showed a large abscess containing 30 to 40 cc. of sanguinopurulent material in the lower lobe, with atelectasis and consolidation of the middle lobe. Microscopic examination of sections through the bronchus intermedius and adjacent lymph nodes showed marked necrosis of the bronchus with infiltration of the bronchus by nonseptate hyphae. The patient was discharged on the 34th postoperative day. Her diabetes was controlled by diet and insulin, and a vaccine made from Candida albicans and Mucor was given 3 times a week.

From similar patients, previously reported, it is apparent that a preexisting severe illness is necessary for the establishment of pulmonary mucormycosis. Diabetes mellitus with acidosis and coma was the predisposing factor in reducing resistance to infection in this patient. With the marked inflammatory reaction and destruction of the bronchial wall, obstruction was produced. This then favored the development of a bacterial abscess distally. The principal factor necessary to effect a cure was control of the diabetes mellitus; removal of the nonaerated destroyed lung was a second essential factor, for this removed an area that harbored an infection and made control of the diabetes possible. The limitation of the fungus infection to the bronchus, followed by normal healing of the bronchial stump, was considered to be due to the rigid control of the patient's diabetes. The fungus was not grown from this patient, possibly because the number of fungi were few as compared with nonhemolytic Micrococcus pyogenes var. aureus and Neisseria sicca grown from the sputum. The fungus in the tissue was confined to a small segment of the bronchus and would surely have grown if a portion of the bronchus had been used as inoculum. Phycomycetes are readily recognized in tissue sections by the masses of nonseptate hyphae and, when invasive into the tissue, may be considered pathogenic.

Neurilemoma Involving Bone. M. S. Hart and W. C. Basom. J. Bone & Joint Surg. 40A:465-468 (April) 1958 [Boston].

The authors report on a 46-year-old man with neurilemoma of the femur. While the patient was playing baseball, his right lower extremity collapsed under him in a deformed position. He was in severe pain and was immediately taken to the hospital. Roentgenograms revealed a long oblique fracture of the upper third of the right femur with a fairly sharply demarcated cystic-like area in the line of the fracture. An open reduction was done. The cystic area, which was about 3 cm. in greatest diameter, was situated at the nutrient foramen. A yellowish-gray, encapsulated dumbbell-shaped tumor, extruding through the cystic area and distorting the adjacent soft tissues and muscle, was dissected with relative ease. The greater portion of the tumor, which measured about 8 cm. in diameter, was adjacent to the muscle belly of the vastus intermedius. A nerve trunk could be seen entering the tumor on its superior medial aspect. The patient had an uneventful postoperative course, and follow-up observations revealed no evidence of recurrence.

On sectioning the operative specimen, there was found distinct lobulation of the tissue, with fibrous trabeculations separating yellowish-gray, firm tissue, but there were many various-sized cystic areas, measuring up to 2 cm., scattered throughout. These were filled with a thin, slightly blood-tinged, mucoid fluid. The cystic linings were smooth. A small nerve could be identified at 1 pole of the mass; this blended into the tumor. Microscopic examination of multiple sections showed interlacing strands of cells with elongated nuclei, often arranged in gentle whorls and sometimes showing typical palisading of the nuclei. In addition, there were typical Verocay bodies. Scattered, thick-walled vessels were interspersed throughout the sections, and there were delicate strands of connective tissue which produced the lobular pattern. From the location of the neurilemoma, it is believed that this tumor arose from a nerve which entered with the nutrient vessel of the bone, producing a destructive lesion at the nutrient foramen which resulted in a dumbbell-shaped tumor. As such, the lesion could be classified as an intramedullary neurilemoma of the femur.

A neurilemoma is a true benign nerve-sheath tumor. It apparently occurs rarely within bone, although it is fairly common in peripheral, cranial, and sympathetic nerves. It may arise from any nerve or nerve root that has a sheath of Schwann and is usually fairly solid. There is a distinct capsulation of a neurilemoma in contrast to a neurofibroma. As the lesion enlarges, cystic changes are characteristic. The lesion rarely recurs if completely excised.

NEUROLOGY & PSYCHIATRY

The Tuberous Sclerosis Complex. R. M. Cares. J. Neuropath. & Exper. Neurol. 17:247-254 (April) 1958 [New York].

Tuberous sclerosis or Bourneville's disease is a rare condition of infancy or youth, with the triad of retarded mental development, convulsions, and sebaceous adenomas of the face. When skin lesions are absent, as in 50% of all cases, clinical diagnosis becomes difficult. The case presented was clinically confused with postpertussis encaphalitis from the 7th month until the patient's death at the age of 25 years. Autopsy disclosed, besides the typical brain changes, hitherto undescribed pulmonic and splenic hamartomas. Delineation of the cerebral lesions was facilitated by utilizing ultraviolet rays. The involvement of numerous organs and tissues supported Moolten's concept of disseminated hamartomatosis as the basis of tuberous sclerosis. The systemic nature of this condition was well borne out by the existence of hamartomas in lungs, liver, spleen, kidneys, and adrenals, together with bony dysplasias of the skull and of 1 hand. Sebaceous adenomas of the face were not found, although an undetermined facial rash had been noted 12 years before. The hamartial tumor most commonly described as accompanying tuberous sclerosis, the cardiac rhabdomyoma, was absent in this case. An abundance of hamartial lesions and dysplasias existed in other areas: the thickened calvarium; bony asymmetry of the hands; lipomesenchymal tumors of the liver, kidney, and adrenals; hemangioma of the splenic pulp; and the hitherto undescribed peculiar miliary alveolar dysplasias in the lungs. Vascular malformation affected branches of the renal artery in a manner resembling cerebral vascular malformations. There was thus abundant evidence of the systemic nature of various tissue dysplasias in the tuberous sclerosis complex, which may be best expressed by the term "hamartoma" coined by Albrecht in 1904 from "hamartenein," i. e., to err.

An Evaluation of Thymectomy in Myasthenia Gravis. J. A. Simpson. Brain 81:112-144 (March) [Part 1] 1958 [London].

Ten years ago it was generally accepted that the myasthenic response indicates 1 of 3 possible "chemical lesions" at the neuromuscular junction: (1) insufficiency of acetylcholine, (2) excess of cholinesterase, or (3) a "curariform" block of transmission, presumably due to a substance carried in the blood. More recently the logical 4th possibility of an abnormality of the motor end-plates of muscle has been postulated. It is difficult to implicate the thymus in any "chemical pathology" of myasthenia gravis with the possible exception of the neuromuscular block theory. The evidence for causal relationship is of 2 types: 1. Thymic extracts may have neuromuscular blocking properties. 2. Operative removal or radiotherapeutic destruction of the gland is followed by significant improvement in patients with myasthenia gravis. The author reviews evidence of the second type. The cases diagnosed as myasthenia gravis at the National Hospital for Nervous Diseases in London since 1934 were scrutinized, and an attempt was made to trace survivors and to determine the fate of those who had died. Most of the patients seen after 1941 were subjected to thymectomy. Four hundred four cases were available for study. All the patients were traced except 12 who were operated on and 18 who were not subjected to surgery. There were 47 patients with thymic tumor.

The study revealed that there is a substantial chance of improvement after thymectomy in all cases. The saving in life is greatest, when the duration of the myasthenia is less than 5 years and no thymoma is present. After 7 years from the onset considerable improvement after operation is less likely, although it may occur, but the risk of death from myasthenia is less whether or not the patient is operated on. Improvement occurs in both sexes and the ultimate distribution of categories is the same, but the extent of improvement is most significant in women, as they would otherwise have a poorer prognosis than men. The prognosis for life remains poor if a thymoma is present, although preoperative radiotherapy may be benificial. Only 1 patient in 3 survives, but the improvement in myasthenia may then be as great as in nontumor cases. The maximum improvement occurs in patients who first show symptoms at an earlier age and who have their operation younger than the average, but the difference is insufficient to influence the selection of patients for operation. Death from myasthenia is more probable in patients requiring large doses of neostigmine, but, if they survive, the ultimate category after operation is not influenced by the preoperative severity.

Neurologic Complications in Sarcoidosis. B. de F. Olivarius. Ugesk. læger 120:434-437 (April 3) 1958 (In Danish) [Copenhagen].

The course in sarcoidosis can be benign with disappearance of the neurological manifestations in weeks or months. The prognosis is most uncertain as soon as there are signs of parenchymal damage to the central nervous system. Even though there have been described cases of this kind in which the symptoms have wholly receded, slight neurological residual symptoms often remain. Sarcoidosis can affect all parts of the central nervous system and appear as a meningitis, a meningoencephalitis, a polyneuritis, or a mononeuritis, with all transitions from disseminated pictures to signs of circumscribed tumor-like forms, and can present difficulties in differential diagnosis. Diabetes insipidus was a prominent feature in 32 out of 136 cases of sarcoidosis with neurological complications reported in the literature. From 1944 to 1956, 10 patients with sarcoidosis in the central nervous system were admitted to the neuromedical department of the Rigshospital. When the diagnosis of sarcoidosis is borne in mind in vague cases of subacute-subchronic meningoencephalitis, it will probably be found that neurological complications in sarcoidosis are not as infrequent as formerly assumed. Since the etiology of sarcoidosis is unknown, treatment is symptomatic. Treatment with steroids of the adrenal cortex seems to give the best hope of improvement of the prognosis. Two typical cases are described, which also illustrate the apparently favorable effect of corticotropin (ACTH) and Meticorten on the neurological manifestations.

GYNECOLOGY & OBSTETRICS

Myeloid Leukaemia Presenting with Postmenopausal Bleeding. B. A. Thompson. Irish J. M. Sc. 6:191-192 (April) 1958 [Dublin].

During the course of anemia signs and symptoms may arise indicating involvement of almost any organ in the body, because leukemic infiltration may appear in any tissue. The author presents the history of a 56-year-old woman who complained of vaginal bleeding of 2 months' duration. The loss of blood was persistent but small in amount. It was accompanied by a profuse vaginal discharge. Recently the patient had had some frequency and pain on micturition and for several days had had lower abdominal pain. Her family physician had been treating her with penicillin and sulfonamides on account of pyrexia during the previous 10 days. Until the onset of these symptoms she had been in good health. Her menstrual history had been uneventful, terminating in menopause at age 50. There was a considerable area of ulceration of the anterior vaginal wall in its upper third. There were isolated ulcers in both lateral fornices and near the urethra. These ulcers had a necrotic surface and an indurated edge and bled readily to the touch. Examination of the blood revealed myeloid leukemia. The patient's condition deteriorated despite blood transfusion. The vaginal bleeding continued, but there was no bleeding from any other site. She died 2 weeks after admission. Primary gynecologic manifestations of leukemia are rare, but the author points out that in 3 cases reported by Wheaton in 1952 myeloid leukemia was associated with menorrhagia; this is in contrast to Whitby and Britton's statement that amenorrhea is common. The author also mentions reports of 2 patients in whom there was uterine infiltration and in whom postmenopausal bleeding was the presenting symptom of leukemia.

PEDIATRICS

Serum-Lipids and Blood-Sugar Levels in Childhood Diabetes.

O. H. Wolff and H. B. Salt. Lancet 1:707-710 (April 5) 1958 [London].

Although it is generally accepted that the lipoprotein level of the serum rises before the development of atheroma, it has not been proved that the rise causes the disease; nor is there any agreement about the precise lipoprotein fraction or fractions that are increased before atheroma develops. In diabetes mellitus there is a tendency for arterial disease to develop prematurely, leading to occlusive coronary disease, retinopathy, or nephropathy, but it is uncertain to what extent these complications are preventable by strict diabetic control. The authors made a study of the levels of lipids and of lipoproteins in the serum of 35 children attending a diabetes clinic. The diabetic regimen included a diet wherein only the carbohydrate was regulated, but an ample supply of carbohydrate was allowed, namely, 200 to 250 Gm. for a child aged 8 to 10 years. All the children received a single injection of insulin-zinc suspension 20 to 30 minutes before breakfast. Blood for analysis was taken at a routine monthly visit to the clinic, neither parent nor child knowing beforehand that any special test would be applied. The clinic took place in the afternoon; hence the blood was obtained 2 or 3 hours after the main meal, which contained 50 to 70 Gm. of carbohydrate. This explains why in many patients the blood sugar level was high, even though the patients were free from diabetic complications, and routine examinations of urine in the patients' homes every morning and night usually indicated good or fair diabetic control.

The blood specimens were analyzed for the levels of sugar in the blood and for the levels of total lipid, lipoprotein-lipid in 3 electrophoretic fractions, cholesterol, esterified fatty acid, and phospholipid in the serum. The mean levels of beta-lipoprotein lipid, cholesterol, and esterified fatty acid in the serum were significantly higher in the children with blood sugar levels above 200 mg. per 100 ml. than in those with levels below 200 mg. per 100 ml. A progressive rise of beta-lipoprotein level in the serum was observed with a rising blood sugar level. In 3 hitherto untreated patients with only moderate or slight ketosis, the initial levels of serum lipid were high, the rise being largely due to the beta-lipoprotein fraction. Under treatment with insulin, as the blood sugar level fell, the level of beta-lipoprotein in the serum also fell; in 2 patients it reverted to normal. One girl, with long-standing diabetes, had a high level of total lipid and beta-fraction in her serum when admitted in coma. Her recovery was complicated by gangrene and peripheral neuritis. Four months after the coma, when the complications were still present, her serum lipoprotein pattern was within the normal limits when the blood sugar level was near normal. In this case the serum lipid abnormality preceded the development of arterial disease but remained reversible despite the persistence of complications. The results support a hypothesis that hyper-beta-lipoproteinemia develops whenever insufficient carbohydrate is available for metabolic needs. The high levels of beta-lipoprotein and cholesterol in the serum resemble those known to precede the development of atheroma in nondiabetic persons. Although the increased amount of betta-lipoprotein has not been proved to cause the early development of arterial complications in juvenile diabetics, the facts strongly suggest the desirability of maintaining normal serum lipid patterns.

Influence of Fasting on the Immunological Reactions and Course of Acute Glomerulonephritis

J. Brod, L. Pávková, V. Fencl and others. Lance 1:760-763 (April 12) 1958 [London].

Fasting has proved to be one of the most effectiv means of treating acute glomerulonephritis. Th acute manifestations, such as reduction of glomerular filtration rate, hypertension, and edema, rapidl subside after fasting. An autoallergic vascular reaction is assumed to be the cause of acute glomerulonephritis. The authors investigated whether fasting interferred with the capacity to produce ar autoallergic reaction. Many victims of concentration camps, who had previously had allergies, los them during their period on a semistarvation diet The autoallergic reaction in acute glomerulonephritis is accompanied by a raised serum titer of certain agglutinins (collodion agglutinins), which may represent antikidney antibodies. The authors studied the change of the titer of these agglutinins in the course of therapeutic fasting in acute glomerulonephritis and compared the course of these changes with the course of the main clinical and functional manifestations of glomerulonephritis. The patients investigated were treated with enforced strict bed rest. Fasting was usually started 24 hours after admission. During the first 24 hours in hospital, the patient was kept on a light diet, and basal data on his renal functions and (in most cases) collodion agglutinins were obtained. The period of fasting lasted 60 hours; the patients received neither food nor fluid, except 100 ml. of unsweetend fruit juice a day.

When the 60-hour period was over. the patients were put on a semistarvation diet, consisting mainly of fruit and vegetables and yielding no more than 500 calories, which was continued until all signs of the acute vascular reaction (reduced glomerular filtration rate, hypertension. and edema) had subsided. Children who served as controls were kept in bed and were given the light diet customarily used in glomerulonephritis, but they did not fast. From the first day of the treatment the glomerular filtration rate was estimated by the clearance of endogenous creatinine in 4-hour periods throughout the whole period of observation. Daily Addis counts of the urinary deposit were made. Blood pressure and fluid balance were measured daily, and the titer of the collodion agglutinins was estimated. The 29 patients with acute glomerular nephritis who were subjected to the fasting treatment included 25 children, between 5 and 15 years of age, and 4 adults. In the fasting group, the agglutinin titer, blood pressure, and glomerular filtration rate all returned to normal significantly sooner than in the controls. In 8 patients with normal initial agglutinin titers, fasting did not shorten the illness. The authors believe that fasting reduces the severity of the antigen-antibody reaction responsible for acute glomerulonephritis and should be an essential part of the treatment.

Familial Congenital Cirrhosis of Liver Due to ABO Blood Incompatibility. H. Garcés, E. Rosenblut, J. Bauza and A. Guzmán. Rev. chilena Pediat. 28:503-507 (Dec.) 1957 (In Spanish) [Santiago, Chile].

The patient was a 1-month-old infant. Her parents, who were first cousins, had never received a blood transfusion. They had 8 children, all of whom but 1, who was slightly premature, were born apparently normal at full term. Five of the infants, including the premature infant, showed moderate jaundice since the third day of birth, moderate anemia, and a rapidly progressive disease of the type of obstructive jaundice secondary to hemolytic disease of the newborn with marked hepatomegaly, splenomegaly, passage of dark urine, pale stools, and rapid aggravation. The infants died between the ages of 12 days and 2 months with a clinical diagnosis of cirrhosis of the liver. Two children are living and are normal at the ages of 9 and 4 years respectively. The older child has moderate hepatomegaly, otherwise, she is normal. The patient had a disease of the same type as the infants who died. A clinical diagnosis of cirrhosis of the liver was made. Inasmuch as hemolytic disease of the newborn was suspected as the cause of the disease, lood-group determinations were made in the famly with the following results: The blood of the her and of the patient was of group A; the blood he mother and of the 2 children who are living as of the O group. The blood of the mother conained a very high titer of anti-A agglutinins. In the lood of the patient there was no erythroblastemia, nd the Coombs direct test gave negative results. ggravation rapidly occurred, and the infant died. utopsy confirmed the clinical diagnosis of cirrhosis f the liver of the type caused by obstructive jaunlice secondary to hemolytic disease of the newborn. The authors believe that cirrhosis of the liver from blood incompatibility between the mother and the infant is caused as follows: The mother becomes sensitized during pregnancy because of the different blood group of the fetus. The antibodies formed in the blood of the mother produce acute hemolysis of the erythrocytes in the blood of the infant, with consequent hyperbilirubinemia, thickening of the bile, precipitation of biliary pigments in the intrahepatic bile ducts, obstruction of the bile ducts, a reaction of interstitial fibrosis of the hepatic cells and damage to the cells, and finally cirrhosis of the liver.

OPHTHALMOLOGY

Infantile Cerebroretinal Lipidosis (Tay-Sachs Disease). S. Gartner and M. Bronstein. A.M.A. Arch. Ophth. 59:584-589 (April) 1958 [Chicago].

This study concerns the type of lipidosis which occurs in infants, in whom swelling of specific nerve cells with granules of a lipid nature exists in the central nervous system and the retina. In the retina the specific portion that is involved is limited to the ganglion cell. This ganglion-cell lipidosis is not confined to the macula but involves ganglion cells of the entire retina. The term "cerebromacular degeneration," which has been used for this disease, is therefore erroneous. Amaurotic familial idiocy describes the effect of the disease, resulting from extensive degeneration of the central nervous system. The term "Tay-Sachs disease" appropriately denotes the original investigators. However, in view of our present knoweldge, the name "infantile cerebroretinal lipidosis" seems more appropriate. Nineteen previously described cases of infantile cerebroretinal lipidosis, in which autopsies have been performed and eyes have been examined post mortem, were identified by such names as the infantile form of amaurotic idiocy, Tay-Sachs disease, and cerebromacular degeneration. Five additional cases of infantile cerebroretinal lipidosis studied histologically at Montefiore Hospital, New York, form the basis of this report. The diagnosis in each case was verified at complete autopsy. The eyes were sectioned at the eye laboratory.

Infantile amaurotic familial idiocy is usually restricted to infants of Jewish extraction, as were 4 of the 5 in this report. There is a familial tendency. Consanguinity plays a part. Onset is about 4 to 6 months of age. There is deterioration of mental processes, blindness, and progressive weakness. About 12 to 18 months is the usual period of survival. The period of survival plays a major role in determining the anatomic changes in the retina. In 3 patients described who survived less than 13 months, there was swelling of some of the retinal ganglion cells, alongside many normal neurons. Ballooned cells were noted throughout the retina, but they were best seen at the macula where they are most numerous. Autopsies in these cases of brief survival revealed similar swelling of cerebral ganglion cells and atrophy of the remaining central nervous system. Retinal ganglion-cell disintegration was more advanced in the remaining 2 patients, with survival of 19 and 34 months respectively. In the more protracted case ganglion-cell destruction was almost complete. Thus, diseased ganglion cells in infantile cerebroretinal lipidosis progress from an early stage of swelling to complete disintegration.

Lipemia Retinalis: Report of a Case in a Diabetic Child Aged Twenty-Eight Months and Review of the Literature. H. W. Laws and E. R. Harpur. A.M.A. Arch. Ophth. 59:521-526 (April) 1958 [Chicago].

Lipemia retinalis is a visible ophthalmic manifestation of a profound disturbance in lipid metabolism. It occurs most frequently in association with diabetes concomitant with acidosis. The 28-month-old boy whose case is presented here shares with 1 presented by Koch and Strong in 1947 the distinction of being the youngest diabetic with lipemia retinalis reported to date. The boy was admitted to the Montreal Children's Hospital in October, 1956. He had been well until 3 weeks prior to admission, when easy fatigability and refusal to play were noted. A week later it was realized that his appetite, previously exceptionally good, had diminished, although he was thirsty and drank up to 2 qt. of orange juice daily. He was weak and lethargic and had deep sighing respirations not associated with respiratory difficulty. He lost weight rapidly and became progressively more lethargic until the day of admission, when he became difficult to arouse. The maternal grandfather was a diabetic at the time of his death, and the mother was said to have had diabetes at 16 years of age, which was cured after 4 years of treatment by diet alone.

On physical examination the child was pale, stuporous, emaciated, moderately dehydrated, and markedly hyperpneic. His liver was grossly enlarged, reaching almost to the umbilicus. The reflexes were diminished. The pupils were dilated but reacted to light. Fundus examination revealed all the characteristics of marked lipemia retinalis equally in the 2 eyes. The disks were a creamy yellow-pink, and the vessels on the disks and extending into the periphery were ivory-colored. Arterioles and venules all looked alike and appeared flat and about twice the normal width. The retina itself was a pale yellowish-pink; there were no hemorrhages. The visual acuity was not assessable because of the patient's age and the presence of coma. Urine examination revealed large quantities of both sugar and acetone. The blood had the appearance typical of pronounced lipemia. Electrophoresis of the plasma showed most of the fat to be neutral fat.

Clearing of the lipemia retinalis began on the 3rd day and was first seen in the vessels of the disks, which began to assume a pinkish color in the center of the lumen while the walls remained pale. By day 4 the pink color of the vessels extended out beyond the disk margin, and the general appearance of the retina became less yellowish. Between day 6 and day 7 the peripheral vessels cleared, and the whole fundus became almost normal in appearance. The child was discharged to the care of his family physician after 17 days. When seen again about 5 months later, he appeared to be in excellent health. His eyes appeared normal, his liver was no longer palpable, and his diabetes was well controlled on 15 units of isophane (NPH) insulin daily.

The authors present a complete list of references, comment on attempts made to explain the phenomenon, and suggest a further explanation—that any preponderance of chylomicrons over red blood cells will tend to reduce the red color of the smaller vessels. If anemia is marked, as in the present case, there may be such dilution of the red blood cells as almost to nullify any red coloration. This would explain why lipemia retinalis is seen first and last in the smaller peripheral vessels and in mild cases is confined to them. Thus, a rising red blood cell count and a decreasing lipemia would account for clearing the lipemia retinalis. Chylomicron and red blood cell counts throughout the illness would evaluate this theory.

THERAPEUTICS

Phenylbutazone in Small Doses in the Treatment of Joint Diseases. E. Jesting, P. Bastrup-Madsen and P. Bechgaard. Acta med. scandinav. 106:305-314 (No. 4) 1958 (In English) [Stockholm].

Phenylbutazone was given to 180 hospitalized patients with various joint diseases in Aarhus, Denmark, between 1953 and 1956. Of these, 71 had osteoarthritis, 52 had rheumatoid arthritis, 20 had atypical arthritis, 9 had gout, and 28 had miscellaneous joint diseases. On the first day of treatment 800 mg. of phenylbutazone was given, followed by 200 mg. daily for various periods of time. With this dose it was possible to maintain a phenylbutazone concentration in the blood of 3 to 4 mg. per 100 cc. In a few patients, the dose of the drug was increased to 400 mg. daily for a short period. Administration of the drug was continued in the patients who showed a satisfactory response; they were discharged for continued treatment at home when this seemed appropriate. The best results were obtained in patients with gout, all of whom showed a good response to the first course of treatment, which was continued until a few days after the subsidence of the attack. In 6 of the 9 patients who were followed for from 2 months to 2 years, it was possible to control all subsequent attacks with the drug. Satisfactory response was observed in 24 of the 71 patients with osteoarthritis, in 10 of the 52 patients with rheumatoid arthritis, and in 8 of the 20 patients with atypical arthritis. In these 3 groups,

WASHINGTON NEWS

FROM THE WASHINGTON OFFICE OF THE AMERICAN MEDICAL ASSOCIATION

Jenkins-Keogh Legislation Making Some Progress in House . .
Efforts Continue for Nursing Home Mortgage Guarantees . .
Consultants Urge U. S. Triple Medical Research Spending . .
Senators are Asked to Lift Restrictions on Medicare . .

PROGRESS MADE ON JENKINS-KEOGH LEGISLATION

Encouraging progress is being made on Jenkins-Keogh bill to help the self-employed set up retirement funds.

The House Ways and Means Committee has amended the legislation to provide the following:

Only the self-employed to be covered.

The amount of money that could be set aside to be limited to 10% of income, but no more than $2,500 in any one year.

The program to be limited to 20 years, in effect placing a ceiling of $50,000 on an individual retirement fund.

A tax penalty of 10% if the money is removed from the fund before age 65.

After the committee had agreed on these provisions, Chairman Wilbur Mills (D., Ark.) said he was confident that the committee would vote out the bill by a "large majority." He expected this action in a few days, but the committee staff encountered difficulty in working out a final draft of the bill, so official committee approval was delayed.

A. M. A. RENEWS APPEAL FOR MORTGAGE GUARANTEES FOR NURSING HOMES

Speaking for the American Medical Association, Dr. R. B. Robins has appealed to the House banking and currency's subcommittee on housing to approve a program of federal mortgage guarantees for proprietary nursing homes. Dr. Robins, a newly-elected trustee of the A. M. A. and a former vice-president, testified similarly before a Senate subcommittee on legislation which subsequently was

tive, [illegible]

that we will not suffer any losses [illegible] cians" by having dependent patients bypass the AF hospitals.

Joining in the appeal to preserve Medicare were American Hospital Association, which filed a statement; the National Medical Veterans Society (Dr. Oscar B. Hunter Jr., testifying for Dr. Milo A. Youel); and the California Medical Association, with Dr. John M. Rumsey as witness.

an increase in quality and quantity of nursing homes would help to ease the cost of old people's medical care by offering them adequate facilities at far less cost than hospitalization.

Earlier, Dr. Steward Hamilton, testifying for the American Hospital Association, endorsed the principle of federal mortgage guarantees but raised several objections to the type of bill passed by the Senate.

He said the AHA objected to including nonprofit institutions because they couldn't afford to meet the contemplated commercial interest charges that were acceptable to proprietary homes. Also, he proposed that the nursing homes be required to qualify under a Public Health Service definition and be certified as to community need by a Hill-Burton type survey.

HUGE INCREASE PROPOSED IN MEDICAL RESEARCH AND EDUCATION

A 10-man consultant group of physicians, medical educators, and research directors in private industry has advised the Secretary of Health, Education, and Welfare on the need for tripling the nation's medical research effort in the next 12 years. That would be at the annual rate of between 900 million and 1 billion dollars for both federal and private spending. And because of the need for doubling the number of professional research workers in this period and for maintaining the present physician-population ratio, another 14 to 20 medical schools should be built, Secretary Folsom was told.

These and other recommendations submitted to the secretary make up the final report of the so-called Bayne-Jones committee named nearly a year ago to study medical research programs of the HEW and their relationship to medical education. The consultants originally had planned to make two reports, but with Mr. Folsom's forthcoming retirement (announced considerably after the group's appointment), the final date was moved up. Mr. Folsom is scheduled to retire in August.

Chairman of the consultants was Dr. Stanhope Bayne-Jones, former medical dean at Yale and now president of the Joint Administrative Board of the New York Hospital–Cornell Medical Center. Also [illegible] Dr. George P. Berry, medical dean at [illegible] owell T. Coggeshall, dean, biological [illegible] of Chicago, and formerly spe-

[illegible] nued on page 26)

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice President.
1958 Clinical Meeting, Minneapolis, Dec. 2-5.
1959 Annual Meeting, Atlantic City, June 8-12.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.

AMERICAN

August

American Congress of Physical Medicine and Rehabilitation, Philadelphia, Bellevue-Stratford Hotel, Aug. 24-29. Dr. Frances Baker, 1 Tilton Ave., San Mateo, Calif., Secretary.

American Hospital Association, Palmer House, Chicago, Aug. 18-21. Dr. Edwin L. Crosby, 18 E. Division St., Chicago 10, Director.

American Veterinary Medical Association, Sheraton Hotel, Philadelphia, Aug. 18-21. Dr. J. G. Hardenbergh, 600 S. Michigan Blvd., Chicago 5, Executive Secretary.

Biological Photographic Association, Shoreham Hotel, Washington, D. C., Aug. 19-22. Miss Jane Waters, Box 1668, Grand Central P. O., New York 17, Secretary.

Chemical Organization of Cells, Normal and Abnormal, Madison, Wis., Aug. 21-23. Dr. J. F. A. McManus, Univ. of Alabama Medical Center, Birmingham, Ala., Chairman.

International College of Surgeons, Regional Meeting, Western Section, The Riverside Hotel, Reno, Nev., Aug. 21-23. For information address: Dr. Leo D. Nannini, 190 Mill St., Reno, Nev.

National Medical Association, Hotel Schroeder, Milwaukee, Aug. 11-14. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Northwest Proctologic Society, Sun Valley, Ida., Aug. 27-29. Dr. John McKay, 645 Medical Dental Bldg., Seattle, Secretary.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 15-17. Dr. John H. Freed, Denver 20, Secretary.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 21-23. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

World Medical Association, Copenhagen, Denmark, Aug. 15-20. Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, Secretary-General.

September

American Academy for Cerebral Palsy, Sheraton-Biltmore Hotel, Providence, R. I., Sept. 25-27. Dr. Raymond R. Rembolt, University Hospitals, Iowa City, Ia., Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 4-6. Dr. E. Stewart Taylor, 4200 E. 9th Ave., Denver 20, Secretary.

American College of Physicians, Mid-West Regional Meeting, Milwaukee, Wis., Sept. 27. Dr. James F. Gleason, 7 S. Oxford Ave., Atlantic City, N. J., General Chairman.

American Fracture Association, Skirvin Hotel, Oklahoma City, Okla., Sept. 29-Oct. 4. Dr. H. W. Wellmerling, 610 Griesheim Bldg., Bloomington, Ill., Secretary.

American Medical Writers' Association, Hotel Morrison, Chicago, Sept. 26-27. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Roentgen Ray Society, Shoreham Hotel, Washington, D. C., Sept. 27-Oct. 3. Dr. C. Allen Good, 200, 1st St., S. W., Rochester, Minn., Secretary.

Colorado State Medical Society, Broadmoor Hotel, Colorado Springs, Sept. 24-27. Mr. Harvey T. Sethman, 1612 Tremont Place, Denver 2, Executive Secretary.

Kansas City Southwest Clinical Society, Municipal Auditorium, Kansas City, Mo., Sept. 22-25. Mr. A. L. Bingham, 3036 Gillham Rd., Kansas City 8, Mo., Executive Secretary.

Kentucky State Medical Association, Brown Hotel, Louisville, Sept. 23-25. Mr. J. P. Sanford, 1169 Eastern Parkway, Louisville 17, Executive Secretary.

Michigan State Medical Society, Sheraton-Cadillac Hotel, Detroit, Sept. 30-Oct. 3. Dr. L. Fernald Foster, 606 Townsend St., P. O. Box 539, Lansing, Mich., Secretary.

Mississippi Valley Medical Society, Morrison Hotel, Chicago, Sept. 24-26. Dr. Harold Swanberg, 510 Main St., Quincy, Ill., Secretary.

Montana Medical Association, Northern Hotel, Billings, Sept. 11-13. Mr. L. R. Hegland, P. O. Box 1692, Billings, Executive Secretary.

Nevada State Medical Association, Elko, Sept. 17-20. Mr. Nelson B. Neff, P. O. Box 188, Reno, Executive Secretary.

New Hampshire Medical Society, Mt. Washington Hotel, Bretton Woods, Sept. 19-22. Mr. Hamilton S. Putnam, 18 School St., Concord, Executive Secretary.

Northeastern Section, American Urological Association, Equinox House, Manchester, Vt., Sept. 12-13. Dr. F. O. Harbach, 831 James St., Syracuse, N. Y., Secretary.

Oregon State Medical Society, Columbia Athletic Club, Portland, Sept. 3-5. Dr. Max H. Parrott, 1020 S. W. Taylor St., Portland 5, Secretary.

Tennessee Valley Medical Assembly, Read House, Chattanooga, Tenn., Sept. 29-30. Dr. Harry A. Stone, 109 Medical Arts Bldg., Chattanooga 2, Tenn., Secretary.

Texas Academy of General Practice, San Antonio, Tex., Sept. 22-24. Mr. Donald C. Jackson, 1905 N. Lamar, Austin, Tex., Executive Secretary.

Tri-State Medical Society, Shreveport, La., Sept. 18. Dr. J. C. Sanders, Sanders Clnic, Kings Highway, Shreveport, La., Secretary.

Utah State Medical Association, Hotel Utah, Salt Lake City, Sept. 9-11. Mr. Harold Bowman, 42 S. Fifth East St., Salt Lake City 2, Executive Secretary.

Vermont State Medical Society, Mt. Washington Hotel, Bretton Woods, N. H., Sept. 20-22. Mr. Getty Page, 128 Merchants Row, Rutland, Vt., Executive Secretary.

Washington State Medical Association, Davenport Hotel, Spokane, Sept. 14-17. Mr. Ralph W. Neill, 1309 7th Ave., Seattle, Executive Secretary.

October

American Academy of Ophthalmology and Otolaryngology, Palmer House, Chicago, Oct. 12-17. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Secretary.

American Academy of Pediatrics, Palmer House, Chicago, Oct. 20- Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill., Executive Secretary.

American Association of Medical Clinics, Palace Hotel, San Francisco, Oct. 2-4. Dr. John R. Hand, 1216 Southwest Yamhill St., Portland, Ore., Secretary.

American Association of Medical Record Librarians, Statler Hotel, Boston, Oct. 13-16. Miss Doris Gleason, 510 N. Dearborn St., Chicago 10, Executive Director.

American Association of Public Health Physicians, St. Louis, Oct. 27-31. Dr. Joseph M. Bistowish, P. O. Box 1117, Tallahassee, Fla., Secretary.

American Association for the Surgery of Trauma, Drake Hotel, Chicago, Oct. 2-4. Dr. William T. Fitts, Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American Clinical and Climatological Association, Otesaga Hotel, Cooperstown, N. Y., Oct. 9-11. Dr. Marshall N. Fulton, 124 Waterman St., Providence 6, R. I., Secretary.

American College of Gastroenterology, Jung Hotel, New Orleans, Oct. 19-25. Mr. Daniel Weiss, 33 W. 60th St., New York 23, Executive Secretary.

American College of Surgeons, Conrad Hilton, Chicago, Oct. 6-10. Dr. Michael L. Mason, 40 E. Erie St., Chicago, Secretary.

American Dietetic Association, Bellevue-Stratford Hotel, Philadelphia, Oct. 21-24. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Heart Association, Fairmont Hotel, San Francisco, Oct. 24-28 Mr. John D. Brundage, 44 E. 23d St., New York 10, Secretary.

American Otorhinologic Society for Plastic Surgery, Conrad Hilton Hotel, Chicago, Oct. 12. Dr. Josepr G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Public Health Association, Kiel Auditorium, St. Louis, Oct. 27-31. Dr. Berwyn F. Mattison, 1790 Broadway, New York 19, Secretary.

American School Health Association, St. Louis, Oct. 26-31. Dr. A. O. DeWeese, 515 E. Main St., Kent, Ohio, Secretary.

American Society of Anesthesiologists, Penn-Sheraton Hotel, Pittsburgh, Oct. 19-24. Dr. J. Earl Remlinger, 802 Ashland Ave., Wilmette, Ill., Secretary.

American Society of Plastic and Reconstructive Surgery, Drake Hotel, Chicago, Oct. 12-17. Dr. Kenneth L. Pickrell, Duke Univ. Hosp., Durham, N. C., Secretary.

Association of American Medical Colleges, Ocean House, Swampscott, Mass., Oct. 13-15. Dr. Dean F. Smiley, 2530 Ridge Ave., Evanston, Ill., Secretary.

Association of Life Insurance Medical Directors of America, Statler Hotel, Hartford, Conn., Oct. 22-24. Dr. Royal S. Schaaf, P. O. Box [illegible] Newark 1, N. J., Secretary.

Association of Medical Illustrators, Dallas, Tex., Oct., Miss Rose M. Reynolds, 42d & Dewey Ave., Omaha 5, Secretary.

Association of State & Territorial Health Officers, Hotel Washington, Washington, D. C., Oct. 22-24. Dr. Mack I. Stanholtz, State Office Bldg., Richmond, Va., Secretary.

Central Association of Obstetricians and Gynecologists, Hotel Leamington, Minneapolis, Oct. 2-4. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

Central Neuropsychiatric Association, Deshler Hilton Hotel, Columbus, O., Oct. 17-18. Dr. Ralph M. Patterson, Ohio State Univ., College of Med., Columbus 10, O., Secretary.

Central Society for Clinical Research, Drake Hotel, Chicago, Oct. 31-Nov. 1. Dr. Austin S. Weisberger, 2065 Adelbert Rd., Cleveland 6, Secretary.

Clinical Orthopaedic Society, Brown Palace Hotel, Denver, Oct. 2-4. Dr. Charles H. Franz, 1801 Wealthy St. S. E., Grand Rapids, Mich., Secretary.

Congress of Neurological Surgeons, St. Francis Hotel, San Francisco, Oct. 29-Nov. 1. Dr. Richard L. DeSaussure, 899 Madison Ave., Memphis, Tenn., Secretary.

Gulf Coast Clinical Society, Pensacola, Fla., Oct. 23-24. Dr. J. J. Baehr, Jr., 117 N. Palafox St., Pensacola, Fla., Secretary.

Indiana State Medical Association, Murat Temple, Indianapolis, Oct. 13-15. Mr. James A. Waggener, 23 E. Ohio St., Indianapolis 4, Executive Secretary.

Pennsylvania, Medical Society of the State of, Bellevue-Stratford, Philadelphia, Oct. 12-17. Mr. Lester H. Perry, 230 State St., Harrisburg, Executive Director.

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